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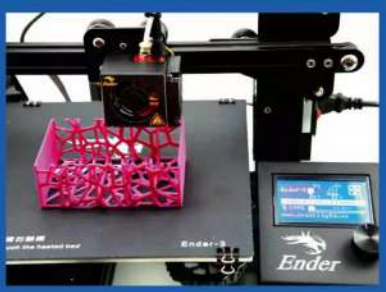

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How similar are turtle shells to human ribs? →p79

FROM THE EDITOR

The first detection of a gravitational wave; the discovery of the first Earth-like exoplanet; the confirmation of the Higgs boson. I've been lucky enough to report on all these and more in the last decade. But in terms of significance, the discovery of CRISPR-Cas9 overshadows them all. No other breakthrough this side of the century has greater potential to shape our future.

If you're not familiar with it, CRISPR-Cas9 is a genetic toolkit that lets biologists remove a snippet of DNA, and potentially insert something new. The act of genetic editing itself is not new, but CRISPR-Cas9 is accurate, quick and cheap, and for the last decade or so scientists have been using it to try to solve some of our biggest problems. There are research groups out there using CRISPR technology to remove malaria from mosquitoes, to engineer drought-resistant crops and to rebuild the planet's coral reefs, to give just a few examples.

But nowhere is CRISPR-Cas9's potential more profound or more controversial than when it comes to treating and curing disease. CRISPR tech can be used to remove pesky bits of our code that can lead to genetic diseases – like sickle-cell disease or blindness – and indeed just last year Victoria Gray became the first patient to be treated by the gene-editing tool. Beyond that, it could even be used to add code to our own DNA to help us fight off infectious disease or deal with chronic pain. It will fundamentally change how we deal with illness. But as is always the question with any new medical breakthrough. Is it safe? And will everyone be able to benefit from its use?

Daniel Bennett

Daniel Bennett, Editor

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BBC Sounds, available now

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Returning for a fourth series, **Our Lives** shares the stories of 12 ordinary people doing extraordinary things around the UK.
BBC One, 11 August, check Radio Times for details

The Life Scientific
Jim Al-Khalili's fantastic radio programme returns in September. He'll be joined by a range of expert guests, including neuroscientist David Eagleman, mathematician Hannah Fry and psychologist Alice Gregory.
BBC Radio 4, starts 7 September

CONTRIBUTORS

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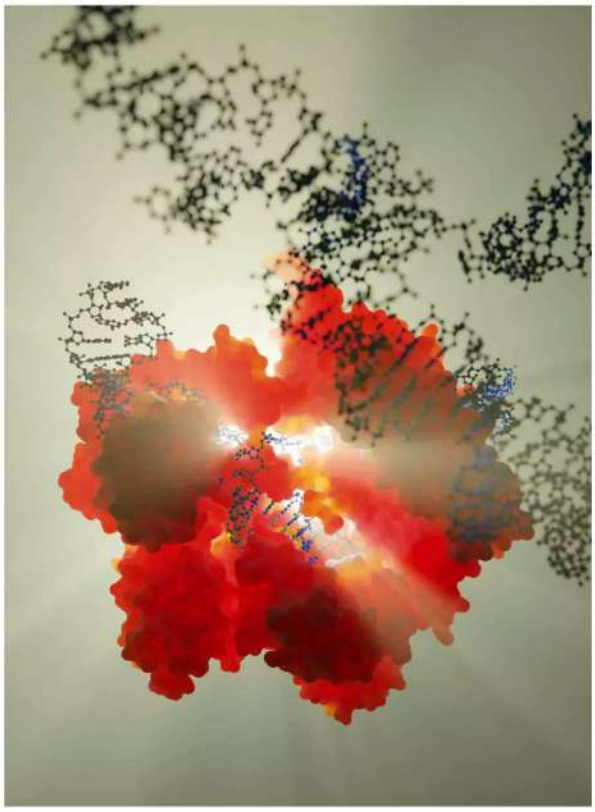

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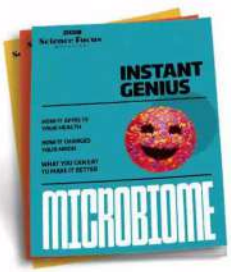

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EYE OPENER

Head in the stars

TELESCOPE LIVE, EL SAUCE OBSERVATORY, CHILE

We often make analogies between deep space and the ocean – the word 'astronaut' is derived from 'star sailor' – but we don't usually expect to find a marine mammal in the sky.

The Dolphin Head Nebula, located 4,530 light-years away, is a bubble of gas and dust that has been blown into this shape by the interstellar winds of the turbulent, dying star in the centre of the image. It was imaged using data from Chile's Telescope Live.

"We can track what's happening in distant nebulae by looking for light signatures. When a gas gets heated, it becomes ionised – meaning an electron gets knocked off the atom – and emits light with a specific colour or wavelength known as a spectral line," says astronomer Dr Elizabeth Pearson. "The H-II line is formed when hydrogen is heated by young, hot stars. By looking for where in the Dolphin Nebula is emitting H-II, astronomers can work out where the nebulae is rapidly forming stars."

YOVIN YAHATHUGODA/APY13

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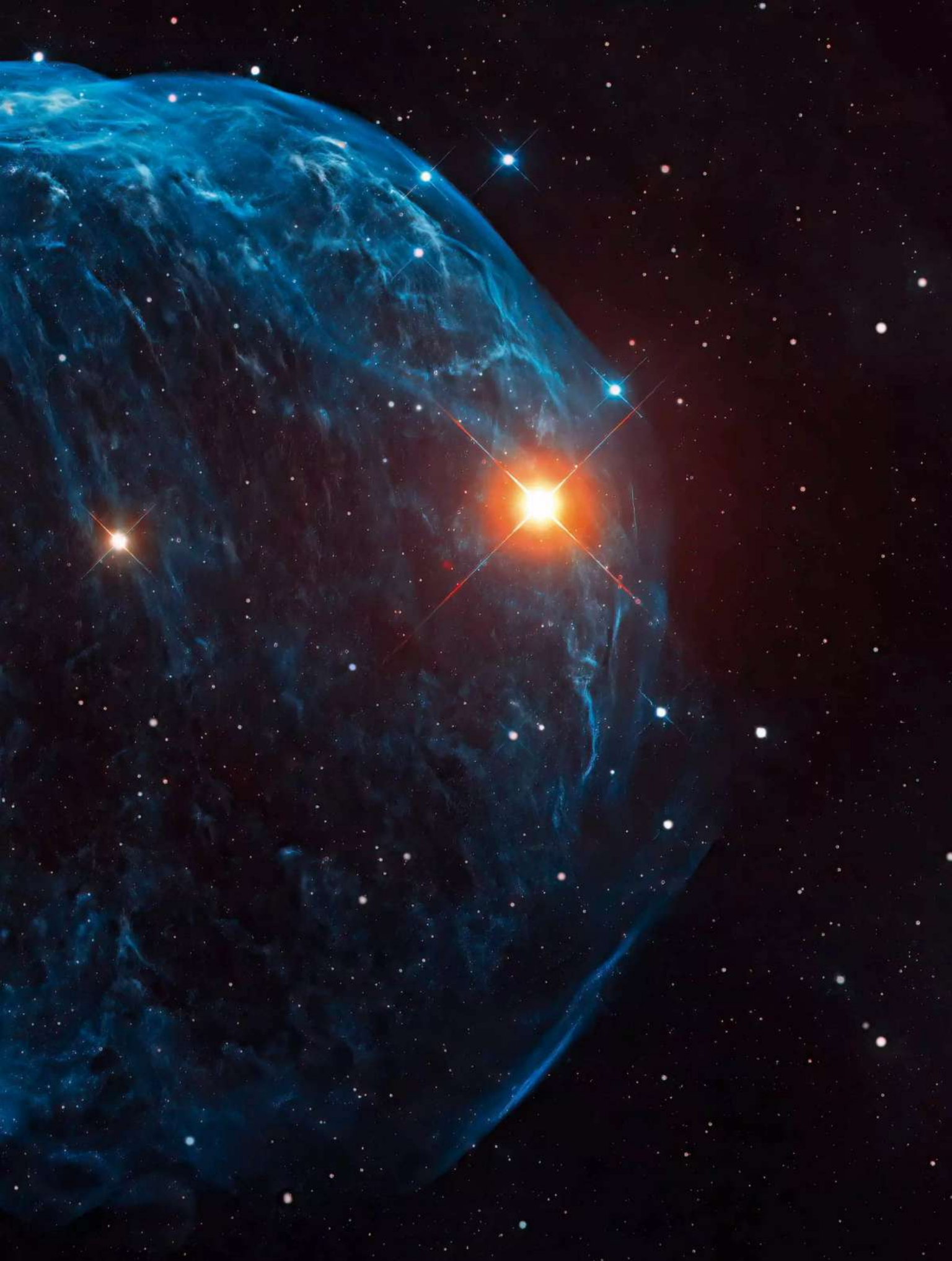

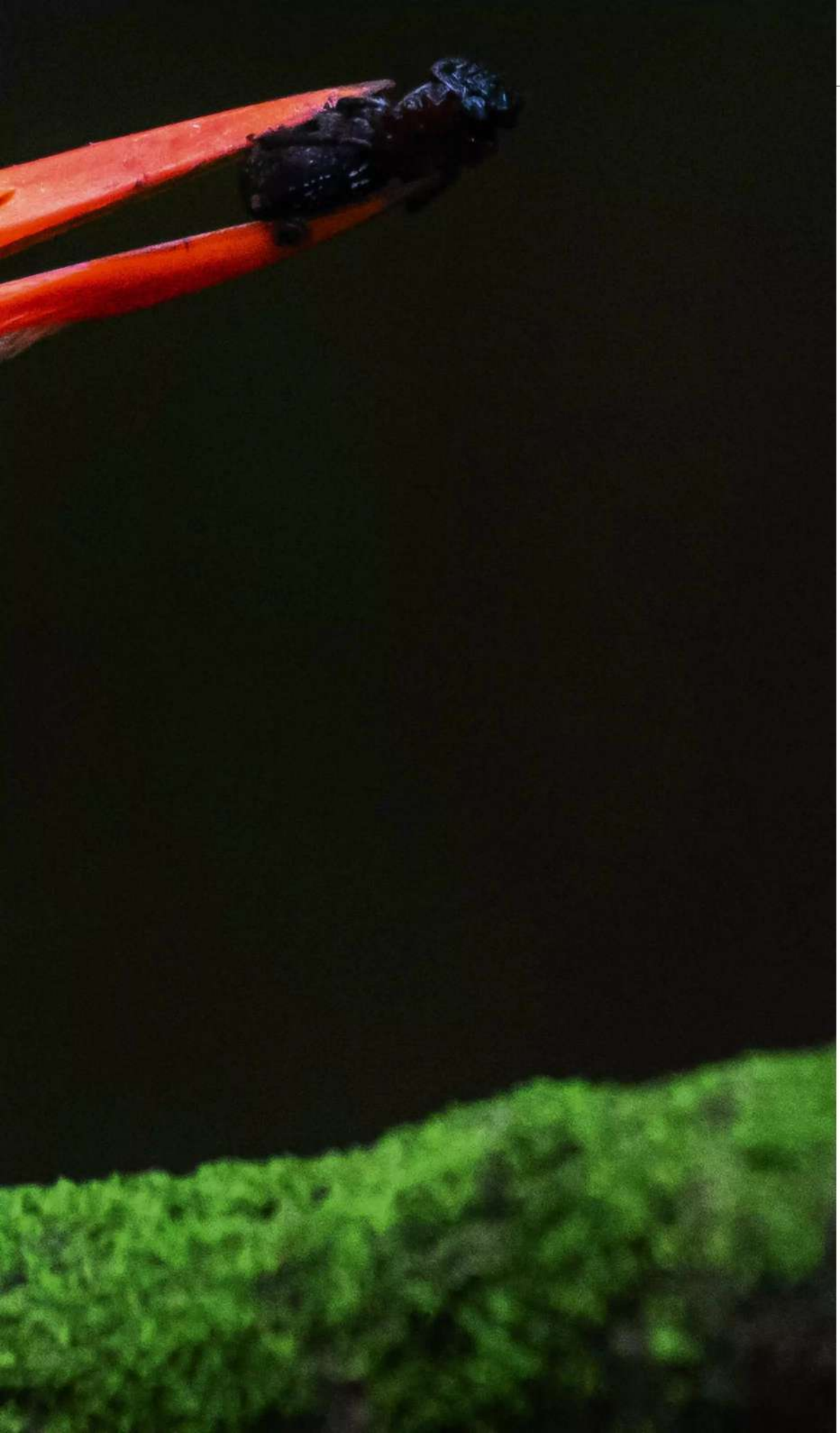

EYE OPENER

Pint-sized predator

PANVEL, INDIA

This beautiful bird is a kingfisher, but it mostly eats insects rather than fish. Oriental dwarf kingfishers inhabit tropical forests in Southeast Asia and the Indian subcontinent, and are miniature, rainbow replicas of the kingfishers we see in the UK, explains Dr Frederick Sheldon, professor of natural science at Louisiana State University. Their bright colours contrast with the dark forest, but at 7.6cm in length they can be hard to spot. "They zoom around the rainforest, flying fast and low to the ground to find their food," he says.

Those who identified the birds discovered that some had a lavender colour on their back, like this one, while others had a deep, dark blue. "It was confusing for people studying them – for years we thought that they were two different species," says Sheldon.

Clarity only came in 2010, when a paper by Sheldon and colleagues revealed it was genetic variation within the species, like eye and hair colour in humans.

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EYE OPENER

‘Ctrl + p’ for pork

BARCELONA, SPAIN

“Honey, get me a new ink cartridge – we’re having steak for tea!”

These thin lines of plant protein may not look overly appetising, but the people behind this 3D meat printer say they can mimic a variety of foods.

“Currently we have beef steaks, pork, and chicken prototypes, but we aim to print different cuts of cow, chicken breast, tuna and more, in the near future,” says Alexandre Campos, business development manager for Novameat.

The ‘ink’ is made from a mix of plant proteins, water, vegetable fats, fibre and ‘natural aromas and colourants’, the exact combination of which has taken extensive testing to perfect. “It has the same nutritional characteristics as a piece of meat, but from plants,” says Campos.

Novameat’s focus, however, is on supplying supermarkets and foodservices with their meat alternatives, so it might be a while before you have a meat printer in your home and need to add ‘ink’ to your shopping list.

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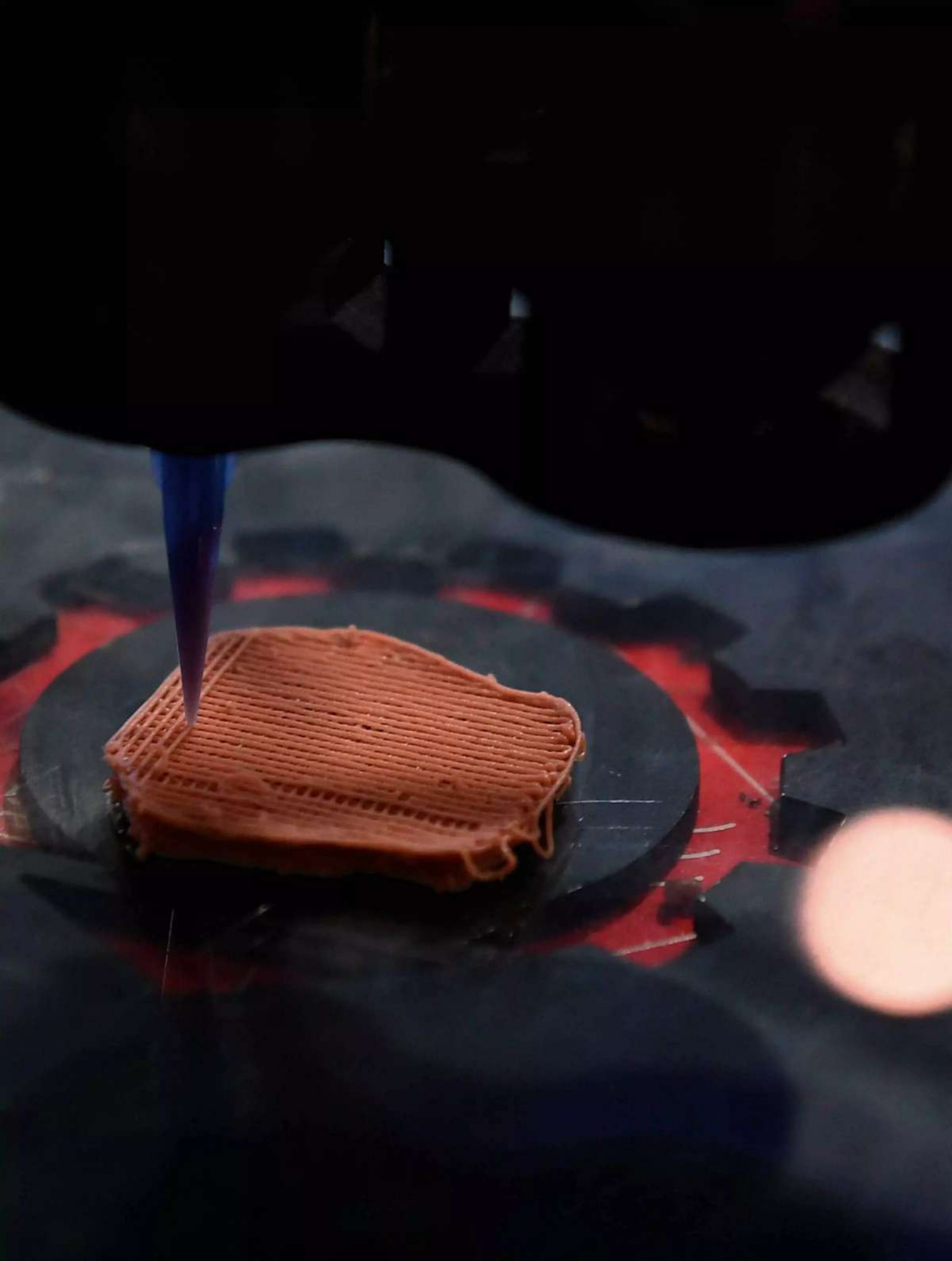

CONVERSATION

YOUR OPINIONS ON SCIENCE, TECHNOLOGY AND *BBC SCIENCE FOCUS*

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LETTER OF THE MONTH

A new unit of area

We often read articles in which a certain area, say a plantation of bananas, would be said to cover Belgium, Cornwall, India, the City of London, and so on. This is not very helpful except as a rough guide, and even then you would need to have an atlas or relevant map with you to complete the comparison.

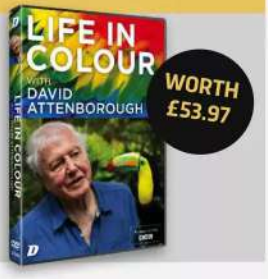
There are standard units of area, such as the acre and the hectare, but how many of us can relate to them? The same applies to the square metre, square kilometre, square mile, etc. Perhaps a very common area that we are frequently exposed to is that of the soccer pitch, so why not use that as the unit of area? It could be the sp and could have sub-units of kilosoccerpitch, ksp, and msp, µsp, and so on.

Now how can we handle '30,000 bacteria can line up along the tip of a needle'?

RJ Minns, Hants

WRITE IN AND WIN!

The writer of next issue's *Letter Of The Month* wins a ***Life In Colour* bundle**. The prize includes a Blu-ray copy of David Attenborough's *Life In Colour*, his book *A Life On Our Planet*, and a triple insulated stainless steel water bottle, for hot and cold drinks on your next nature walk. *Life In Colour* with David Attenborough is out now on Blu-ray, DVD and download-to-own.



Real big question

I read in Marcus Chown's article (June, p52) that physicist Stephen Wolfram proposes that space is made up of a network of 'nodes' that are connected to each other, and that our fundamental limitations do not permit us to see these 'atoms of space', but instead a smooth continuum. Could this be seen as leaning back towards the idea of 'the ether medium' which was widely searched for in the late 19th Century but rejected by Einstein when developing his theory of General Relativity?

Stephen Dixon

Green issue

In the June issue (p80), you show a chart that misleadingly paints a warm, rosy picture over what is in fact a global disaster. It shows China, followed by Australia and then India, as countries with increasing forest areas. The main issue is one of how the data is interpreted. It depends on what you mean by 'increasing forest cover'. The system that is used to show this can be open to

A rescued baby wallaby, whose mother was killed in the Australian bushfires in 2020

"[WITH CRISPR] THERE CAN BE MISCONCEPTIONS EMBEDDED IN THE PUBLIC MINDSET THAT CAN HAVE A NEGATIVE EFFECT ON WHAT I THINK SHOULD BE POSITIVE ADVANCES"

DR JENNIFER DOUDNA, P52

Could prosthetic limbs one day offer benefits over 'natural' limbs, ponders Richard

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misinterpretation. It may show an increase in regrowth by saplings, but it does not show that this comes at the cost of cutting down mature forest and old-growth forest. And with that comes massive loss of life of native animals and destruction of pristine habitat.

Wildlife took a massive hit in last year's forest fires in Australia, which pretty much everyone on the planet agrees is due to global warming, and yet the cutting down of old growth forests in Tasmania and land clearing in Queensland for cattle grazing continues.

Simply planting new trees is not the answer. Keeping what we still have would be a much better solution.

Carel Lucas

Gaming the system

In the Summer 2021 edition (p80) the top 10 list shows that non-human animals can easily outperform us in a wide range of sports. Are there any animals who could outperform humans in multi-activity sports such as the pentathlon?

You also discuss how technology has improved performance in sport. In future there will probably be a dilemma when, for example, prosthetic limbs enable people to run/jump/swim better than athletes with 'natural' limbs. How could this affect categories in both the Olympics and Paralympics? And could athletes be tempted to have amputations to enhance their careers?

Richard

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ANNUAL SUBSCRIPTION RATES (INC P&P):
UK/BFPO £77; Europe & Eire £92.54;
Rest of World £102.90.

Audit Bureau of Circulations
45,132 (combined, Jan-Dec 2020)

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THE AMAZON NOW EMITS MORE CARBON THAN IT ABSORBS

Fires burned in the forest tipped the balance this year

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Fires in the Amazon are set deliberately by farmers to clear land for agriculture

The Amazon rainforest is now emitting more carbon than it is able to absorb, a study by a team of international researchers has found.

For generations, the vast area of forest, often referred to as the 'lungs of the Earth', naturally absorbed carbon dioxide in the air. But now, the researchers say it is putting out around one billion tonnes of carbon dioxide more a year than it can absorb.

The whole Amazon basin comprises about half of the planet's tropical rainforests, though the study only covered the forests found in Brazil, which make up about 60 per cent of that figure.

The emissions are largely driven by fires set by developers deliberately burning down the trees to clear agricultural land for the grazing of cattle or the growing of soy beans, the researchers say. Over the last 40 years, the conversion of the natural landscape to agricultural land has caused a 17 per cent decrease in rainforest in the Amazon. This has caused the forests to dry out, which can reduce their capacity to store carbon and increase their vulnerability to fires.

> **"The Amazon is starting to become sick. It's not a good sign"**

"An important message is that essentially it shows that these forests are starting to suffer," said one of the study's authors Prof Emanuel Gloor, from the University of Leeds. "And that's not good because these forests are not only important because of the carbon cycle, but they are important also because of this enormous biodiversity that is there.

"We have already destroyed so much on the Earth, and in a way, this shows that we could say that the Amazon is starting to become sick. It's not a good sign. We know that there is deforestation, so it's not really a surprise, but one could say it is large-scale proof that things are not going in a good direction."

The team used an aircraft to fly above the Amazon to measure the carbon dioxide and carbon monoxide over several areas of the Brazilian rainforest from 2010 to 2018. They found that fires produced around 1.5 billion tonnes of carbon dioxide per year on average, while new growth could only account for removing around 0.5 billion tonnes.

While breaching the carbon emission tipping point may seem dire, there is still time to reverse the trend, they say.

"I would say with the foremost urgency do not support any products or agricultural products that originate from newly destroyed forests," said Gloor. "But my hunch would be that it is possible to halt this. But I do think in places where large-scale deforestation has happened, the forests might not return very rapidly."

SPACE

Astronomers spot moon-forming rings around a baby exoplanet

For the first time, astronomers have detected a dusty ring around an exoplanet where moons could be born. They hope the discovery will teach us more about how both planets and moons are formed.

The newly forming exoplanet PDS 70c orbits a star almost 400 light-years from Earth, along with protoplanet PDS 70b. PDS 70c was discovered with the European Southern Observatory's Very Large Telescope in 2019. Previous studies found hints that it may have a moon-forming disc around it, but astronomers have now confirmed it, thanks to new, high-resolution images from the Atacama Large Millimetre/submillimeter Array (ALMA).

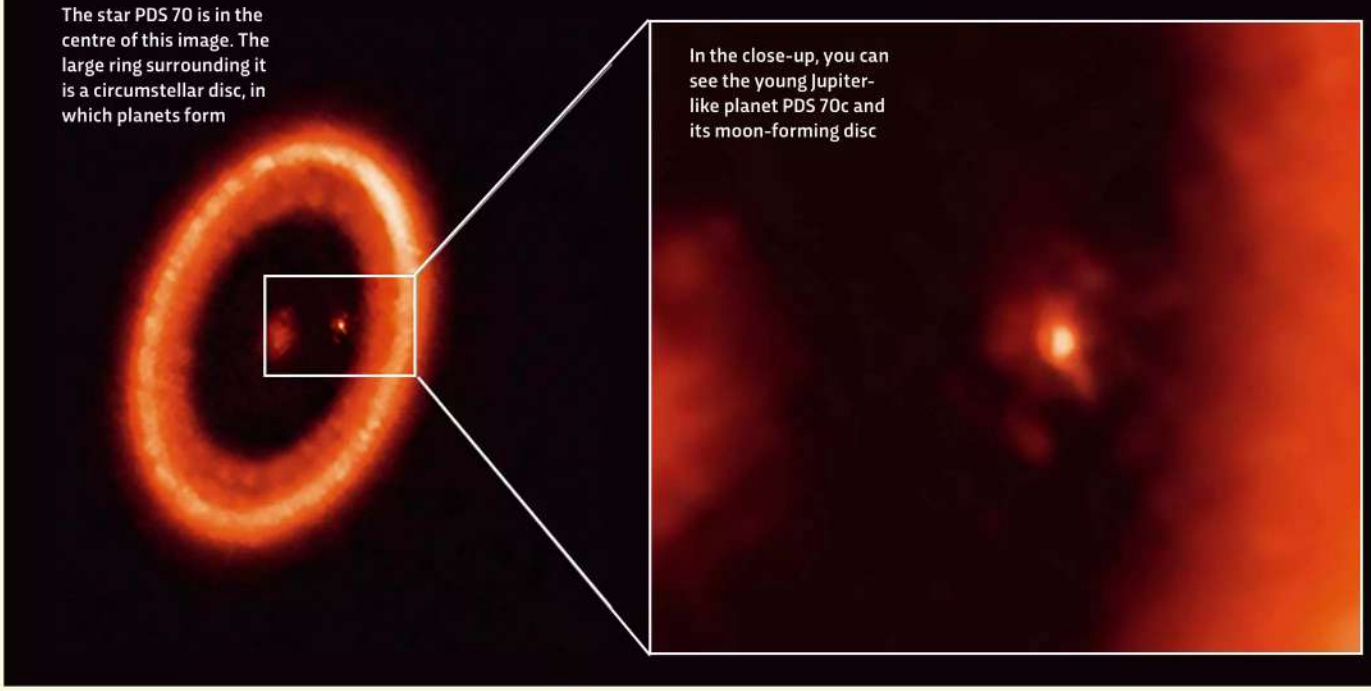
"Our work presents a clear detection of a disc in which satellites could be forming," said Dr Myriam Benisty, at the University of Grenoble, France and the University of Chile. "Our ALMA observations were obtained at such exquisite resolution that we could clearly identify that the disc is associated with the planet and we are able to constrain its size for the first time."

The disc has a diameter roughly equal to the distance between the Earth and the Sun, and it contains enough mass to create a satellite the size of our Moon three times over.

Since the planet is so new, it could reveal not only how moons are created, but also how planets are formed. Planets are born around new stars from a large disc of dust and gas. As a planet begins to coalesce, it starts to form its own disc, and a moon can emerge out of this dust and gas.

"More than 4,000 exoplanets have been found until now, but all of them were detected in mature systems," said Dr Miriam Keppler, a researcher at the Max Planck Institute for Astronomy in Germany. "PDS 70b and PDS 70c, which form a system reminiscent of the Jupiter-Saturn pair, are the only two exoplanets detected so far that are still in the process of being formed."

Since systems like these are so rare, there is a lot that astronomers don't yet know about planet formation. "It is still unclear when, where and how planets and moons form," said ESO research fellow Stefano Facchini. "This system therefore offers us a unique opportunity to observe and study the processes of planet and satellite formation."



The star PDS 70 is in the centre of this image. The large ring surrounding it is a circumstellar disc, in which planets form

In the close-up, you can see the young Jupiter-like planet PDS 70c and its moon-forming disc

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HEALTH

A fungal vaccine could boost your microbiome and prevent gut disease

Many people, from your mum to Instagram health gurus, have touted the benefits of having some friendly bacteria in your guts. However, little is said about the balance of your intestinal fungi, which could have just as much impact on your health. At least, that's what's been shown by an intriguing new study from the University of Utah Health.

In experiments with mice, researchers found that while fungi can thrive in a healthy gut, they may also cause intestinal damage leading to inflammatory bowel disease (IBD). To reach this finding, the researchers analysed the makeup of the yeast *Candida albicans* – one of the main species of fungi that are found in the human gut – in the intestinal systems of mice.

They discovered that although the mice populated with the yeast in its normal state were healthy, mice filled with the filamentous form (known as hyphae) experienced damage resembling IBD. The researchers also found that the immune systems of healthy mice targeted the fungi when it switched to its filamentous state, inhibiting disease from forming.

"The immune system is constraining *Candida* to its least pathogenic form," explained Dr Kyla Ost, the study's lead author. "It shows us that the communication between host and microbe can be friendly, as opposed to antagonistic."

But that's not all. The researchers theorised that a vaccine could be developed in future to protect patients against IBD.

Mice prone to an IBD-like condition were found to be less likely to develop the disease when administered with a vaccine currently designed as a remedy for vaginal yeast infections. The scientists are now working on a vaccine that could mitigate IBD in people and improve their gastrointestinal health.

"This study reveals new insights into how host antibodies preferentially allow the non-invasive form of *Candida* to grow, and could lead to therapies which can help to keep *Candida* in a commensal [friendly] state," said Dr Elisabeth Lowe from the Biosciences Institute at Newcastle University, who was not involved in the study. "This is really important for patients who we know are at high risk of invasive *Candida* infection, such as those on immune-suppressants."

This study is part of the growing understanding of how fungi could be used to improve the microbiome of humans – and their overall health.

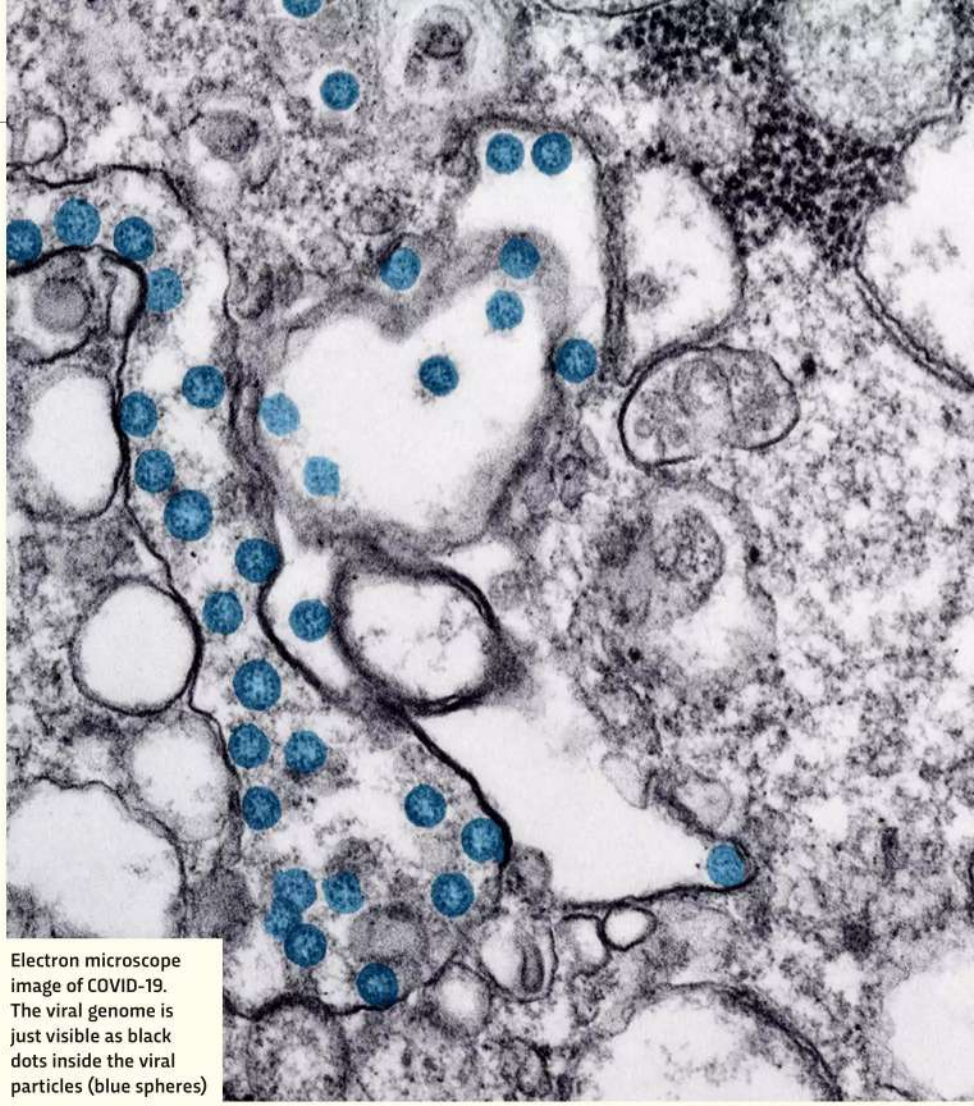
"Fungi are a crucial part of our gut microbiomes that play a key role in our immune defences, but have been hard to measure," said Prof Tim Spector, an epidemiologist at King's College London and author of *Spoon-Fed*, who was not involved in the study. "The next few years should show us how to harness their potential to prevent diseases and how to manipulate them with diet."

Candida lives on the skin and in the body, and can cause issues, particularly in immunocompromised people

MEDICINE

How we could turn COVID against itself

In the red corner, a 'wild-type' SARS-CoV-2 virus. In the blue corner, a defective interfering SARS-CoV-2 virus. Now, 3, 2, 1, FIGHT!



Electron microscope image of COVID-19. The viral genome is just visible as black dots inside the viral particles (blue spheres)

GETTY IMAGES X2

For the last 18 months we have been washing our hands, wearing masks and vaccinating to fight the coronavirus. But could we make the virus do battle with itself and fight COVID with COVID?

Researchers at Penn State University have designed a proof-of-concept treatment that might be able to do just that.

Viruses thrive because they invade the cells of other organisms, forcing them to create viral proteins and genetic material so the virus can replicate, before bursting out of the cell to start the whole process again.

The team at Penn State designed a synthetic version of the SARS-CoV-2 virus that interferes with the real virus's growth. They say that it could potentially wipe out both the 'real' virus and the synthetic version.

"In our experiments, we show that the wild-type [disease-causing] SARS-CoV-2 virus actually enables the replication and spread of our synthetic virus, thereby effectively promoting its own decline," said Marco Archetti, associate professor of biology at Penn State. "A version of this synthetic construct could be used as a self-promoting antiviral therapy for COVID-19."

According to Archetti, these 'defective interfering' (DI) viruses are common in nature, and contain large deletions in their protein-coding genes that hinder their ability to replicate themselves. However, if they manage to infect a cell that also contains a 'wild-type' virus, they can hijack its machinery and replicate themselves. When a DI virus uses wild-type virus machinery, it can also impair the growth of the wild-type virus. Thanks to their shorter genome, DI viruses could even replicate faster, outcompeting the wild-type virus.

> "This synthetic DI could be used as a therapeutic for COVID-19"

To carry out the study, the team took a SARS-CoV-2 genome and used it to engineer synthetic DI genomes. They then introduced these DI genomes to monkey cells that had been infected with wild-type SARS-CoV-2.

After 24 hours, the DI genome had replicated three times faster than the wild-type, and viral load was reduced by half.

Archetti says that while a reduction of half in 24 hours is not enough for therapeutic purposes, further experiments need to be carried out. In unpublished research, the scientists have tried using nanoparticles as a delivery vector, and saw the virus decline by more than 95 per cent in 12 hours.

"With some additional research and fine-tuning, a version of this synthetic DI could be used as a self-sustaining therapeutic for COVID-19," said Archetti.

"This is an interesting proposal. However, it is unlikely this would ever be a viable way to stop the spread of COVID-19," said Dr Jeremy Rossman, a virologist who was not involved in the research. "First, we don't know if a DI SARS-CoV-2 virus would prevent all human clinical disease, including long COVID. Second, the use of any live virus as a therapeutic has to ensure that continued virus evolution does not risk the DI virus causing disease or changing how the regular version of the virus behaves. Third, for the DI virus to inhibit the normal version, the same person has to be simultaneously infected with both versions. Infection with the defective version would not persist in a person until they got subsequently infected and so it is unlikely this would be a viable way to stop COVID, though it is an intriguing concept."

In numbers

7 per cent

The proportion of the modern human genome that is unique and not shared with our early ancestors.

4.9 million tonnes

The amount of carbon trapped in soil that is released by wild pigs annually. That's the equivalent of one million cars.

319 terabits per second

The new record for data transmission set by scientists at Japan's National Institute of Information and Communications Technology (NICT).

GETTY IMAGES X2

HEALTH

Look after your teeth to protect against cognitive decline in old age

With each lost tooth, the risk of cognitive impairment grows – but not for those who have dentures

Tooth loss is linked to cognitive decline and dementia, a study at NYU Rory Meyers College of Nursing has found. However, the researchers did not see the same effect in older adults with dentures.

The team analysed 14 studies on the link between tooth loss and cognitive function, involving a total of over 34,000 adults. They found that tooth loss was linked to a 1.48 times higher risk of cognitive decline, and a 1.28 times higher risk of dementia, even after they controlled for other factors.

However, those who had dentures did not have the same risk. In fact, the researchers found no significant link between tooth loss and cognitive decline in people with dentures. People with missing teeth were more likely to be cognitively impaired if they didn't have dentures.

"Given the staggering number of people diagnosed with Alzheimer's disease and dementia each year, and the opportunity to improve oral health across the lifespan, it's important to gain a deeper understanding of the connection between poor oral health and cognitive decline," said co-author Dr Bei Wu at NYU Rory Meyers College of Nursing.

Previous research has shown a link between oral health and cognitive impairment and dementia, though it's not clear what causes it. Some researchers have suggested that missing teeth may cause difficulty chewing, which could lead to nutritional deficiencies in the brain. Other studies have pointed to a link between gum disease and Alzheimer's disease. Alternatively, it could be that tooth loss is a symptom of socioeconomic deprivation, which is also a risk factor for cognitive decline.

The researchers additionally found that each lost tooth raised the risk of cognitive impairment by 1.4 per cent and dementia by 1.1 per cent. They call this a 'dose-response' association – that is, the greater the cause (tooth loss), the greater the effect (cognitive decline).

"This 'dose-response' relationship between the number of missing teeth and risk of diminished cognitive function substantially strengthens the evidence linking tooth loss to cognitive impairment, and provides some evidence that tooth loss may predict cognitive decline," said co-author Xiang Qi, a doctoral candidate from NYU Meyers.

The researchers suggest that good oral hygiene may even be protective. "Our findings underscore the importance of maintaining good oral health and its role in helping to preserve cognitive function," said Wu.

PETS

Dogs won't give you food, even if you gave them some first

They may be your best buddy, but they won't go out of their way to do you a favour

Dogs are more than just pets; they're a member of the family… right? If so, you'd think that they'd want to look after you just as much as you look after them. But, unfortunately, a study has found that this may not be the case.

Dogs won't give food to a human, even if that person gave them some food first, researchers at the University of Veterinary Medicine in Vienna, Austria, have found.

Previous studies have shown that dogs recognise cooperative and uncooperative humans, and that they would help dogs that had helped them previously. So, the team expected to find that their test subjects would put these two things together and show 'reciprocal altruism' – that is, doing a good thing in return – to a human who had given them food first.

First, the team trained 37 dogs to press a button which would activate a food dispenser. They then put the dog in an enclosure with the dispenser, while one of two humans was in a separate enclosure with the button. One would press the button to dispense food for the dog, and the other would not. Each dog was paired with both humans in turn.

Then, the researchers switched over the button and the dispenser. They expected that the dogs would press the button to give food to the helpful human, but not the unhelpful one. Surprisingly, while the dogs did press the button sometimes, they did it just as often when either human had the food dispenser, and even when no human was there at all.

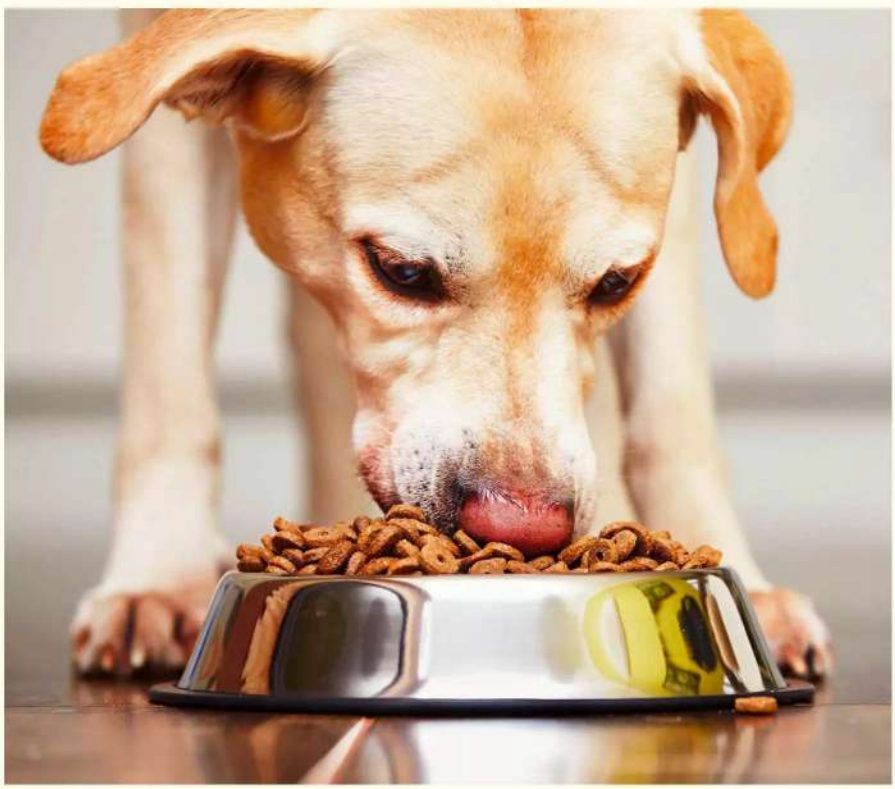
"In these kinds of studies in which dogs are trained to perform a particular behaviour for use in an experimental condition, they will usually perform the behaviour a few times as they have simply learned the association between the behaviour and getting a reward, and it may be enjoyable for them to perform the behaviour," said Jim McGetrick, a PhD student at the University of Veterinary Medicine in Vienna, who led the research.

"So although they did press the button and the human did get food on some trials, this was not because the dogs were trying to provide food to the human."

Why wouldn't our best pals want to help us out by giving us some food? Are they secretly all bad boys and girls? McGetrick believes there is a combination of reasons. "It is possible that the dogs did not understand enough about the task to realise that one human was providing them with food and the other wasn't," he said. This could either be because they didn't fully understand the button and dispenser system, or 'inattentional blindness' – that is, they were too focused on the food to notice whether a particular human was pressing the button or not.

"Having said all that, even if they did understand the task fully and were fully attentive to the actions of the humans, there is still a good likelihood that they wouldn't have reciprocated," he added. "It could be that providing food to a human is something very strange for a dog as they do not typically do that in everyday life." After all, humans are the ones who already have food, from a dog's perspective – why would your pet need to worry about making sure you have enough?

However, all the humans in the study were people the dogs didn't know. "It is quite possible that the results reflect the bond – or lack thereof – between the dogs and the humans in the study," said McGetrick. So yes, your pup really does love you, and it's possible they'd help you out in a pinch, too.



PALAEONTOLOGY

Just-hatched pterosaurs may have been able to fly

Pterosaurs, a group of flying reptiles that zipped around the Earth 228 to 66 million years ago, may have been able to fly as soon as they hatched, research from the University of Portsmouth has found.

A team of scientists studied four previously unearthed hatchling and embryo fossils from two pterosaur species, *Pterodaustro guinazui* and *Sinopterus dongi*. They compared wing measurements, along with the size and strength of the humerus bone, with those of adult pterosaurs of the same species.

"These tiny animals – with 25cm wingspans and bodies that could neatly fit in your hand – were very strong, capable fliers," said study co-author Dr Mark Witton. "Their bones were strong enough to sustain flapping and take-off, and their wings were ideally shaped for powered, as opposed to gliding, flight. However, they would not have flown exactly like their parents simply because they were so much smaller: flight capabilities are strongly influenced by size and mass, and so pterosaur hatchlings, being hundreds of times smaller than their parents, were likely slower, more agile fliers than the wide-ranging, but less manoeuvrable adults."

The researchers found that while hatchlings had long, narrow wings suited to long-distance flight, their wings were shorter and broader than those of adult pterosaurs, with a larger wing area relative to their mass and body size. This means that the hatchlings were likely to be less efficient than mature pterosaurs at long-distance travel, but may have been more agile on the wing and capable of nimble, abrupt changes in direction and speed.

This may have made them better suited to chasing nimbler prey and flying among dense vegetation than adult pterosaurs, the researchers say.

"That gives us a lot to think about with regard to flying reptile ecology," explained Witton. "How independent were the hatchlings from their parents? Did flight style influence habitat choices, and did these change as pterosaurs grew? There's still a lot to learn about the life histories of these animals, but we're confident that, whatever they were doing as they grew up, they were capable of flying from the moment they hatched."

> **"Whatever they were doing as they grew up, they were capable of flying from the moment they hatched"**

Artist's impression of a flock of *Pterodaustro guinazu*, with hatchlings flying alongside adults

The opossums clinging to their mum. From left to right: wild-type, albino and mosaic

DR MARK WITTON, RIKEN CENTER FOR BIOSYSTEMS DYNAMICS RESEARCH

BIOLOGY

Opossum becomes world's first genetically engineered marsupial

The gene-editing tool CRISPR has been used to modify the genes of everything from squid to tomatoes. Now we can add marsupials to the ever-expanding list, as a team at RIKEN Center for Biosystems Dynamics Research in Japan have used it to tweak the genes of a South American species of opossum to change its colour.

Most of the previous research in the field has focused on switching off the genes of mice and rats in order to determine their function. However, as marsupials have a number of unusual genetic quirks compared to other mammals, they present biologists with a unique opportunity to study everything from reproduction and foetal development to immunology and cancer.

The opossum, which is thought to be the ancestor of all marsupials, was chosen as it is the first marsupial to have its entire genome sequenced and has breeding characteristics similar to those of mice and rats.

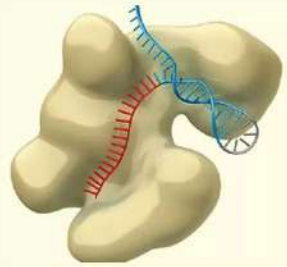
"Marsupials represent one of three extant mammalian subclasses with a number of unique characteristics not shared by other mammals," said research leader Dr Hiroshi Kiyonari. "Having established the technology in this proof-of-concept experiment, future studies can create genetically modified marsupials that will impact the fields of mammalian embryology, genomic imprinting, reproduction, neurobiology, immunogenetics, cancer biology, and even comparative evolution."

In this experiment, the team obtained fertilised eggs from female grey short-tailed opossums, and targeted a gene that is known to be responsible for producing the colour of the animals' skin and fur. When this gene is turned off using the CRISPR technique, the opossums are unable to produce pigment, so their fur and skin lacks colour. The eggs were then implanted into surrogate mothers.

The first litter of animals the team produced using the technique included one albino and one 'mosaic' opossum with mottled fur. They then bred the two animals to produce a litter of fully albino opossums to prove that the colouring was an inherited genetic trait.

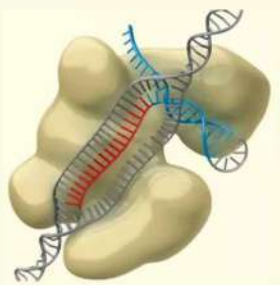
Following their success, the researchers now plan to investigate other aspects of opossums' unique biology.

How CRISPR works



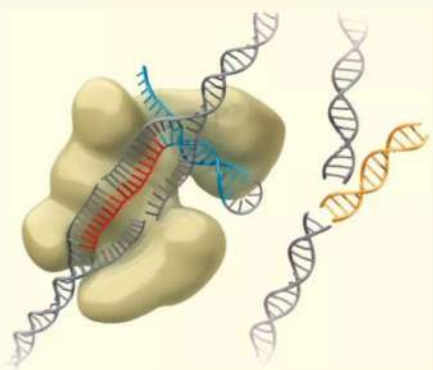
1

The CRISPR molecule is attached to 'Cas9' (shown here in beige). Cas9 is an enzyme that uses its RNA 'guide' to recognise a target DNA sequence.



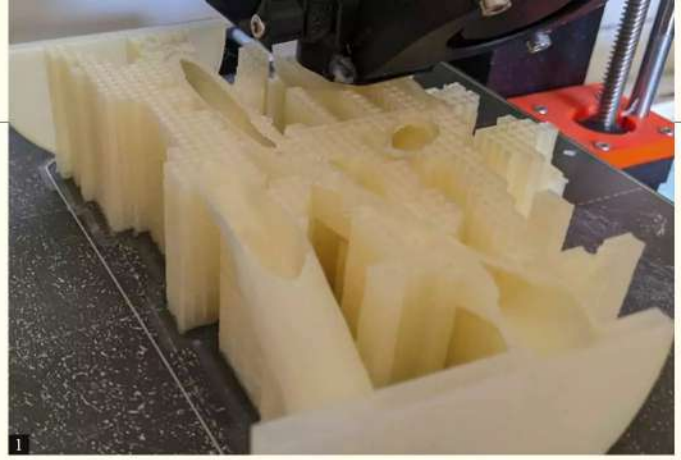
2

The CRISPR-Cas9 tool cuts the strands of the target DNA's double helix. Then the cell's repair machinery will fix the damage.



3

The CRISPR technique can be used to delete unwanted DNA, or to find and replace a sequence by adding genetic material – such as a new gene.



MEDICINE

3D-printed liver models will help surgeons 'rehearse' cancer surgeries

Scientists at Nottingham Trent University have developed a method of using scans of cancer patients' organs to 3D print realistic models so that surgeons can rehearse procedures before they take place in real life. The technique recreates the individuality of a patient's organ, with blood vessels, tissue and any tumours all being included in the completed model.

NOTTINGHAM TRENT UNIVERSITY X5

1. The model liver was constructed using existing 3D scan data taken from an anonymous cancer patient.

2. The team used a combination of synthetic fibres and gels to 3D print an accurate model of the organ, layer by layer.

3. As the process accurately recreates an organ's internal structure, the model allows surgeons to use real tools to practise complicated procedures such as endoscopies.

4. The completed liver model has a texture similar to that of a real diseased organ, including different tissue hardnesses in the blood vessels, liver tissue and the tumour itself. It is filled with imitation blood, to make it as realistic as possible. The organ could even provide trainee surgeons with the opportunity to learn how to remove tumours.

5. Senior research fellow Richard Arm demonstrates how a surgeon might practise an operation on the 3D-printed organ prior to performing the surgery on a living patient. "Every patient is unique and has organs of different shapes, sizes and constructs, so there can be many hidden complications that they [the surgeons] have to deal with," he said. "But this research shows how existing scan data and modern 3D-print processing methods can dramatically improve the preparation available before the first incision is even made."

PROF JILL BANFIELD
Geomicrobiologist

Horizons

Enigmatic DNA 'Borgs' that assimilate genes from host cells found lurking in wetland soil

The discovery could lead to the development of CRISPR-like gene editing tools, the researchers say

YOU'VE DISCOVERED SOMETHING YOU'VE CALLED 'BORGS'. WHAT EXACTLY ARE THEY?

All organisms have a genome. In fact, things that we don't necessarily think of as living organisms have genomes too. People will be familiar with viruses, for example, or maybe plasmids. These rely on other organisms to replicate, to make copies of themselves to survive and propagate.

The Borgs are a kind of DNA-based entity – we can't call them an organism – that lives with and depends on a kind of organism called an 'archaean'. To put that in context, all life on Earth classifies into one of three major groups: bacteria, like *E. coli*, for example; eukaryotes – you and plants and fungi are all eukaryotes; then the third group are archaea. They're much less studied, but really interesting. They were originally thought to be extremophiles, meaning they live in extreme environments. But now we know that they're kind of everywhere. Most recently, it's become clear that these archaea were probably the ancestors of eukaryotes. We all go back to archaea at some point in our history.

WHY DID YOU NAME THEM AFTER THE BORG FROM *STAR TREK*?

There are two ways that evolution happens. One is from parent to child, and child to their child, that's called vertical descent. So you inherit your genome from your ancestors. And then there's another way that organisms can innovate and change and get new capacities, and that's called lateral gene transfer. It's a really important second way of evolution. It means genes can actually move around independent of organisms. Things like viruses are actually kind of important in that process. It's not unusual to have that process happening, but the Borgs seem to be particularly involved in acquiring genes from organisms and inserting them into their own genomes [a bit like how the Borg in *Star Trek* assimilate different species, cultures and technology]. So that's why we call them Borgs.

AND THEY WERE FOUND IN THE SOIL IN YOUR BACKYARD?

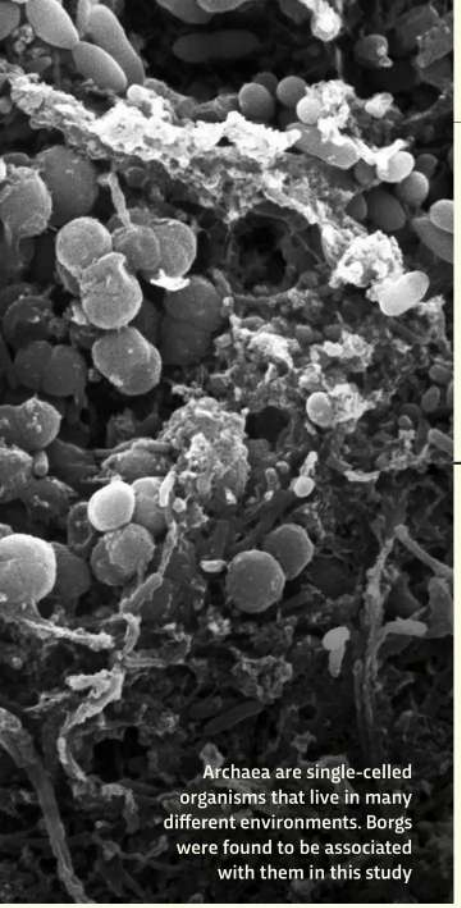
I have a pretty big backyard. I'm living at the moment in the country and we have what's called a vernal pool. It's a pool that fills with water in the springtime and then dries out over the course of the year. We were studying in a nearby area, and we thought, "Oh, why don't we just take some samples from this vernal pool soil and just see if they're interesting." We work in lots of different environment types, studying life's diversity and other things. It made sense to take some samples in a place that's rarely sampled.

HOW MANY DIFFERENT TYPES OF BORG HAVE YOU FOUND?

We have 19 pretty well described Borgs and four others that we are pretty sure about. I feel fairly confident that there are a lot of others out in the world that just haven't been identified to date. The 19 different species of Borg all have somewhat different capacities, but they share common features.

ONE OF THE BORGS YOU'VE STUDIED COULD BE USED TO 'EAT' METHANE IN SOIL TO HELP FIGHT CLIMATE CHANGE. TELL US MORE.

First of all, let's talk about where methane comes from. Essentially, all methane is coming from archaea called methanogens, which just means organisms that make methane. They live in places where there's no oxygen. They live in the subsurface where it's dark and moist, and they're very common in wetlands. They're also common in places like rice paddies. Archaea that make methane exist under the ground, the methane is a gas and it can rise through the soil and enter into the atmosphere. As a greenhouse gas, it causes warming.



Archaea are single-celled organisms that live in many different environments. Borgs were found to be associated with them in this study

ALAMY

"Some of these methane-eating organisms do not have Borgs, but the ones that do appear to have a sort of turbocharged metabolism"

But there are also organisms for which methane is actually pretty good food, they eat the methane. So it's a balance between the organisms that make methane and the organisms that eat it. A lot of different kinds of organisms can eat methane. But a very special kind can also live without oxygen. And they live in the deep subsurface as well. They haven't been known for all that long, but they're really, really, really important. These organisms are the kinds of organisms that are the hosts for the Borgs. And as soon as the methane gets generated, they can eat it. And that prevents its release to the atmosphere. Some of these methane-eating organisms do not have Borgs, but the ones that do appear to have a sort of turbocharged metabolism due to the presence of the Borg. They therefore have extra capacity to consume the methane and generate energy from it. That's why they're important.

ARE THERE DIFFERENT USEFUL FUNCTIONS THAT THE DIFFERENT BORGS CAN PERFORM?

The ones we know now do seem to be involved with adding to the metabolism of their hosts. So, there are two ways of looking at that question. The first is: do completely different organisms have Borgs that do different things altogether? And the answer is, we don't know but it's quite possible, we just need to look for them. We haven't found any yet. But I mean, it would be strange if this is a phenomenon of biology that only occurs in one tiny group. The second question you might be asking is: do the Borgs have other capacities that aren't to do with methane that might be useful? And the answer is absolutely yes, because the most striking feature of these Borgs is that they have on the order of a million genes. We can only predict functions for a small subset of those – most of the genes are completely novel. And so there's a lot of questions you can ask about what they might be doing with those genes, and probably it's got something to do with their existence in a cell within a host.

Having lots of novel genes is not in itself that unusual because most viruses and bacteria, for example, are packed with genes of unknown function. But it does represent a huge potential for discovery of all sorts of interesting capabilities. One thing I think that makes people comprehend the potential significance a little better is to point out that the CRISPR system, which is now renowned for its capacity to edit genomes, came from microbes. It was a bunch of genes of unknown function. And actually, interestingly, it's a system of unknown function that became apparent because of its repeats; the CRISPR system has got sequence repeats in it. That's what was really the flag that said there's something interesting here (read more about CRISPR on p52). And the Borg genomes are full of interesting and enigmatic repeats. I would say there are some good reasons to be looking at these genomes for new biotechnologically relevant tools.

WHAT ARE THE NEXT STEPS?

Well, we plan to do a lot of different things, the first part of this is to answer some pretty fundamental questions. If you've seen any of the Twitter chats, there's been a huge debate about whether these are, in fact, viruses. Some people say they're viruses and other people say they're plasmids. And other people say we can't really classify them as either, they are something new. I don't know if that's all that important because in some ways it's a matter of nomenclature.

But underneath all that is the fundamental question of, do they exist in the cell continuously like a plasmid would? So basically exist alongside a living cell and just be part of the whole cell's set of capacities, or are they more like a virus that comes and infects and kills the cell and then goes away? They are very different patterns. And I think understanding that is a key in understanding what these are and where to turn next to study them.

The second question is related to the tools that might arise. Are there other systems we can discover? We are going to be looking into that. I'm hoping to be able to work with collaborators at UC Berkeley to identify systems, genes and proteins that we think we can predict a function for and see if we can figure out how they're working.

The third thing is to do with the climate. The institute that I'm associated with, the Innovative Genomics Institute at UC Berkeley, has recently launched an initiative on climate and the topic is closely linked to greenhouse gas emissions. And one of the things we are interested in is whether or not we can learn enough about places where greenhouse gases are being formed, such as rice fields, to devise strategies to enhance the growth of organisms that will eat the methane in the soil before it goes into the atmosphere.

PROF JILL BANFIELD

Jill is a professor of microbial metagenomics based at the University of California, Berkeley.

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REALITY CHECK

SCIENCE BEHIND THE HEADLINES

Larks vs owls | Beaver culls | Lockdown and memory

REVIEW

LARKS VS OWLS: ARE PEOPLE WHO WAKE UP EARLY REALLY HAPPIER?

Does early to bed, early to rise make you healthy, wealthy and wise? Here, a neuroscientist explains which people are happiest

"Lark emotional advantage manifests in greater satisfaction with life and reduced vulnerability to mental health problems"

BBC *Visit the BBC's* Reality Check *website at* **bit.ly/reality_check_** *or follow them on Twitter* **@BBCRealityCheck**

Don't you envy those people who bounce out of bed early in the morning with a spring in their step? Or maybe you are lucky enough to be one of them! The early bird catches the worm, so they say, and pop culture is filled with variations on the theme that early risers do better in life and get more done, usually with a smile on their face. Countless articles promise us that if only we could drag ourselves out of bed an hour earlier in the morning, we'd become super productive, just like leading entrepreneurs.

If you're a night owl who prefers to stay up late and nest under the duvet in the morning, you might be hoping it's not really true. But in fact, the psychology of 'chronotypes', as it's known, largely backs up the popular image of early rising, happy go-getters; though, as ever, the reality is a little more nuanced.

ARE MORE PEOPLE LARKS OR OWLS?

The majority – around 60 per cent – of us are not larks or owls, we're an intermediate mix of the two. Another factor to consider is that chronotype isn't just about the time you go to bed and get up in the morning, it's also about your optimal time of functioning. Larks tend to be at their best earlier in the day, while owls tend to function better later on, which could have obvious advantages for certain career paths involving evening work or night shifts.

As for who fits into which grouping, women generally tend to be of the morning chronotype, whereas men are more often the evening chronotype.

Age is another factor. In adolescence, there's a tendency to shift towards the owl chronotype, but after adolescence, lark-like morningness tends to become more common with increasing age.

As for who is happier, many studies have indeed shown an association between being a morning person and greater happiness. For a recent example, consider a study of hundreds of medical students conducted at Dokuz Eylul University in Turkey – higher scores in morningness (a self-reported preference for getting up early) were associated with scoring higher on a questionnaire measure of happiness. Put differently, the 26.6 per cent of students categorised as owls scored lower on happiness than the group (6.7 per cent) categorised as larks, as well as the remainder of students categorised as intermediates. Studies of older people similarly show an association between morningness and greater happiness.

ARE THERE OTHER BENEFITS TO BEING A LARK?

According to a study carried out at the University of Leipzig, lark emotional advantage manifests in greater satisfaction with life and reduced vulnerability to mental health problems. Other studies suggest that people who are owls are more likely than larks to experience depression, seasonal affective disorder and substance abuse problems. Complicating the issue, this difference might be at least partly explained by people who are owls tending to have less sleep or more sleep problems, rather than there being something advantageous about being a lark *per se*. Other possible mechanisms explaining the lark advantage are they seem to have better emotional regulation skills and a more positive attitude toward time.

CAN I CHANGE MY CHRONOTYPE?

All of this raises questions about where our lark or owl-like tendencies come from, and relatedly, but perhaps more importantly, whether we can change them. As a team at the University of Warwick ●

BELOW Larks are generally happier than owls... just don't expect them to go out dancing until dawn

GETTY IMAGES X2

Owls do not cope well in the mornings

showed recently, chronotype is related to personality – being a lark is associated with scoring higher on the trait of conscientiousness (one of the Big Five traits that's associated with being more self-disciplined, orderly and ambitious). Conversely, scoring higher in extraversion and openness is associated with being more of a night owl. In turn, personality and chronotype share some of the same underlying genetic influences, the team showed.

The good news is that neither personality nor chronotype are set in stone. Both are shaped by factors beyond our genes, such as our family environment and professional roles and the routines they demand of us. This malleability implies, as the University of Warwick researchers put it, "...it might be possible to change one's chronotype in a more intentional way." Some basic tips to shift toward being a lark include avoiding using digital devices in the evening, gradually aiming to go to bed earlier, and giving yourself something rewarding to get up for in the morning – be that a freshly brewed coffee, a leisurely walk or a spell of me-time on your iPad.

The bad news is that preliminary findings from the University of Warsaw, based on a study of undergrads, suggested that a seasonal-based shift in chronotype towards greater morningness (in the summer months) wasn't associated with gains in mood and life satisfaction. This suggests that changing your chronotype might not be a quick fix to becoming happier. In part that's probably because the causal direction between chronotype and happiness flows just as much in the other direction, from happiness to chronotype. If you can find contentment in life, and your days are busy and rewarding, you'll probably find it that much easier to get to sleep on time at night and fly, free as a lark, out of bed each morning.

—

by DR CHRISTIAN JARRETT

Christian is a cognitive neuroscientist turned science writer and author. He is the senior editor for Psyche, *the new wellbeing site from* Aeon *magazine. His latest book is* Be Who You Want *(£14.99, Robinson).*

ANALYSIS

BEAVER CULLING: HOW WILL IT AFFECT REWILDING PLANS?

A Scottish legal battle over licences to shoot beavers is setting the scene for a fresh debate on how the reintroduction of native species should be managed

In June, rewilding charity Trees for Life brought a case against NatureScot, Scotland's nature conservation agency, for allowing farmers to kill wild beavers. It argues that NatureScot is breaking the law by granting beaver control licences too liberally.

The judicial review is seen as a key test case for rewilding campaigners who want beavers to spread

GETTY IMAGES, ALAMY

ABOVE In 2020, a demonstration was held in Edinburgh to protest at the number of wildlife species that are dwindling in numbers

> **"There are very few beavers and there is an abundance of land to which they could be relocated"**

further across Scotland and are pushing for the reintroduction of predators such as lynx.

Steve Micklewright, chief executive of Trees for Life, says his organisation believes licences to kill beavers should only be issued as a last resort when all other options, including relocation, have been considered.

"We also believe that if lethal control licences are required, the number of beavers that can be shot under each licence should be stated, rather than left unlimited," he adds.

But NatureScot says these control licences are needed in specific situations, such as when beavers pose a risk of serious damage to farmland or result in a public health and safety concern.

"We are confident that our approach to managing these impacts is robust and lawful and licences are only used if we are satisfied that there is no other solution," says Robbie Kernahan, NatureScot's director of sustainable growth, in the organisation's statement on the review.

The first wild beavers were released in Scotland in 2009 as part of a controlled trial in Knapdale on the western coast. However, a far larger population of beavers has been established in Tayside following an unauthorised release some 20 years ago. Here, their impact on prime agricultural land has caused tensions with farmers.

Dr Helen Senn, head of conservation and science at the Royal Zoological Society of Scotland, one of the partners of the Knapdale beaver trial, notes that dam-building by beavers increases wetland habitat, benefitting a whole host of species.

"However, if this occurs near productive farmland, farmers may lose valuable crops or infrastructure," she says.

The Scottish government has agreed to allow beavers to spread naturally across Scotland. From May 2019, it designated them a protected species, meaning land managers need to obtain a licence from NatureScot in order to kill them or destroy their dams or lodges.

NatureScot granted 40 of these control licences in 2019, with cull returns indicating that 87 beavers were killed, equal to a fifth of the country's total population in 2017 when the last survey was done (the figures for 2020 have not yet been released).

The National Farmers Union (NFU) Scotland, which is supporting NatureScot to oppose the judicial review, defended the licence system, calling it "appropriate and proportionate".

"To those impacted by beavers on their land, the licence system has been a valuable way of protecting their farm from economic and environmental damage," says a NFU Scotland spokesperson.

Beavers and people can co-exist happily in some locations, they argue, but when they arrive in highly productive agricultural areas they can undermine river banks, damage protective flood banks and block farmland drainage.

But wildlife campaigners argue lethal licences are not necessary as there are other options.

Beaver dams can create wetland habitat

Louise Ramsay, from the family-run rewilding project at Bamff Estate in Perthshire, said she understands why certain farmers find beavers problematic but does not think any should be shot in the UK at the moment.

"There are very few beavers and there is an abundance of land to which they could be relocated from situations where they cannot be accommodated," she says.

Some farmers also need to think more about the environmental impact of their farming, and consider whether there are actions they can take to reduce the negative impacts of beavers, she says.

Dr Alan Law, a lecturer in ecology at the University of Stirling, says beavers have become important in the UK's rewilding movement. He says the outcome of the judicial review could have an impact on the reintroduction of other species in Scotland, such as lynx.

"Nature's at breaking point, if not broken already. Rewilding and reintroduction of species is absolutely essential to bring back animals that provide us with natural functions and services in the environment," he says. "If the government loses the review, it will have to re-evaluate its approach to protected species, ensuring it explores all other options before allowing their killing."

The ruling could take up to three months, with a decision from the judge expected by the end of August.

"It will be very interesting to find out what the outcomes are," says Law. "But regardless, I'm hoping everyone can still move forward in an amicable way, and still recognise the benefits of the beavers."

—

by JOCELYN TIMPERLEY

Jocelyn is a freelance climate journalist, based in Costa Rica.

ANALYSIS

COVID-19: HOW HAS LOCKDOWN AFFECTED OUR MEMORIES?

Feel like your memory has deteriorated since the beginning of lockdown? Don't worry, you're not the only one...

From 'poor' to 'excellent', how do you rate your memory before you began social distancing? And how do you rate your memory today? These are two of the questions PhD student Natan Feter and colleagues, from the Universidade Federal de Pelotas in Brazil, posed in their recent study examining the relationship between memory and social distancing measures. It's a question that's been on many people's minds lately: how has lockdown affected our memories?

Feter's team found that roughly one-third of adults from southern Brazil reported worse memory since the beginning of social distancing restrictions. Given that Brazil has never had a national lockdown, and has taken a different approach to the pandemic to most other countries, can such results translate to the UK? To examine this question, Prof Catherine Loveday, a neuropsychologist based at the University of Westminster, set up a study asking people to rate their memory related to everyday tasks. In an interview with BBC Future, Loveday said that preliminary results show that 80 per cent of participants said their memory had deteriorated during the pandemic.

But have you also been getting less exercise over the course of the pandemic? It turns out this might be related to your memory woes. In the Brazilian study, those who remained or became physically active during periods of social distancing were found to be far less likely to report that their memory had worsened, even when adjusted for various other factors, including age. But how physically active did people need to be to see the benefits? It turns out that each extra minute of exercise people did during periods of social distancing meant that they were a bit less likely to report memory declines. In Loveday's UK study, the results were even found for those who were active in ways that we don't tend to think about – people benefitted even just from moving more regularly between rooms or buildings.

And it's not just the physical brain-boost of exercise either. Moving to a different spot gives your brain a change of scenery as new inputs and environments help keep our memories more distinct.

ALAMY, GETTY IMAGES

"Each additional step, roll, or shuffle, particularly into a new environment, may make you feel less like your memory is slipping away during socially distanced periods"

Together, these findings are all in line with the United Nations' COVID policy brief that pointed out that reduced physical activity is a risk factor for cognitive decline and dementia, particularly for older adults. So, each additional step, roll, or shuffle, particularly into a new environment, may make you feel less like your memory is slipping away during socially distanced periods.

Of note is that both of these studies measured subjective memory decline. This means that people said that they felt like their memory was worse. But *feeling* like your memory is worse isn't the same as your memory *being* worse. So, does this subjective feeling match reality? And do we know whether social distancing is really making us descend into a foggy forgetfulness?

Earlier this year, the University of Otago's Dr Weiwei Zhang and colleagues published a paper in which they asked 374 participants from the UK and US how many days in a row they had socially distanced before participating in a word memory task. They found a U-shaped relationship between social distancing and memory errors. This means that, counterintuitively, memory errors initially slightly decreased as social distancing duration increased. So, for the first bit of lockdown their memory for words was better than before lockdown. It was only after an average of 30 days that memory errors began to steadily increase.

The team also found an almost perfect relationship between mood and memory. As mood dipped, so did memory. Loneliness was particularly potent in decreasing how well people remembered words, which understandably increases as time goes on and is also associated with a risk of dementia. This is yet another reason why reaching out to connect with each other during periods of social distancing can help to keep our brains and memories in good shape.

Finally, how good are we at remembering experiences that happened during the entire pandemic period, rather than just in a day-to-day setting or in wordlists? Dr Norman Brown, a cognitive psychologist based at the University of Alberta, has proposed 'transition theory' to help us understand the possible effects of the pandemic on autobiographical memory. The theory predicts that there is a COVID bump and a lockdown dip. The COVID bump is an increase in the memories of events for the beginning of the pandemic. The lockdown dip is a decrease in the memories of events for the lockdown periods. This means that we are probably good at remembering things that were rapidly evolving and extremely emotional in the early weeks of the pandemic, while we are bad at remembering what happened during the lockdown periods where our days were tediously similar.

ABOVE Losing things more often? Struggling to find the right word? Many people have reported memory lapses during the pandemic period

So, what's the verdict? Does lockdown negatively affect our memories? Probably. The effect might be related to your negative mood, or that you haven't returned to your exercise routine. Consider changing the room, or even part of the room, in which you work to help to mitigate your brain fog. Most importantly, it seems that being extra forgetful during lockdown is temporary rather than permanent. Phew. **SF**

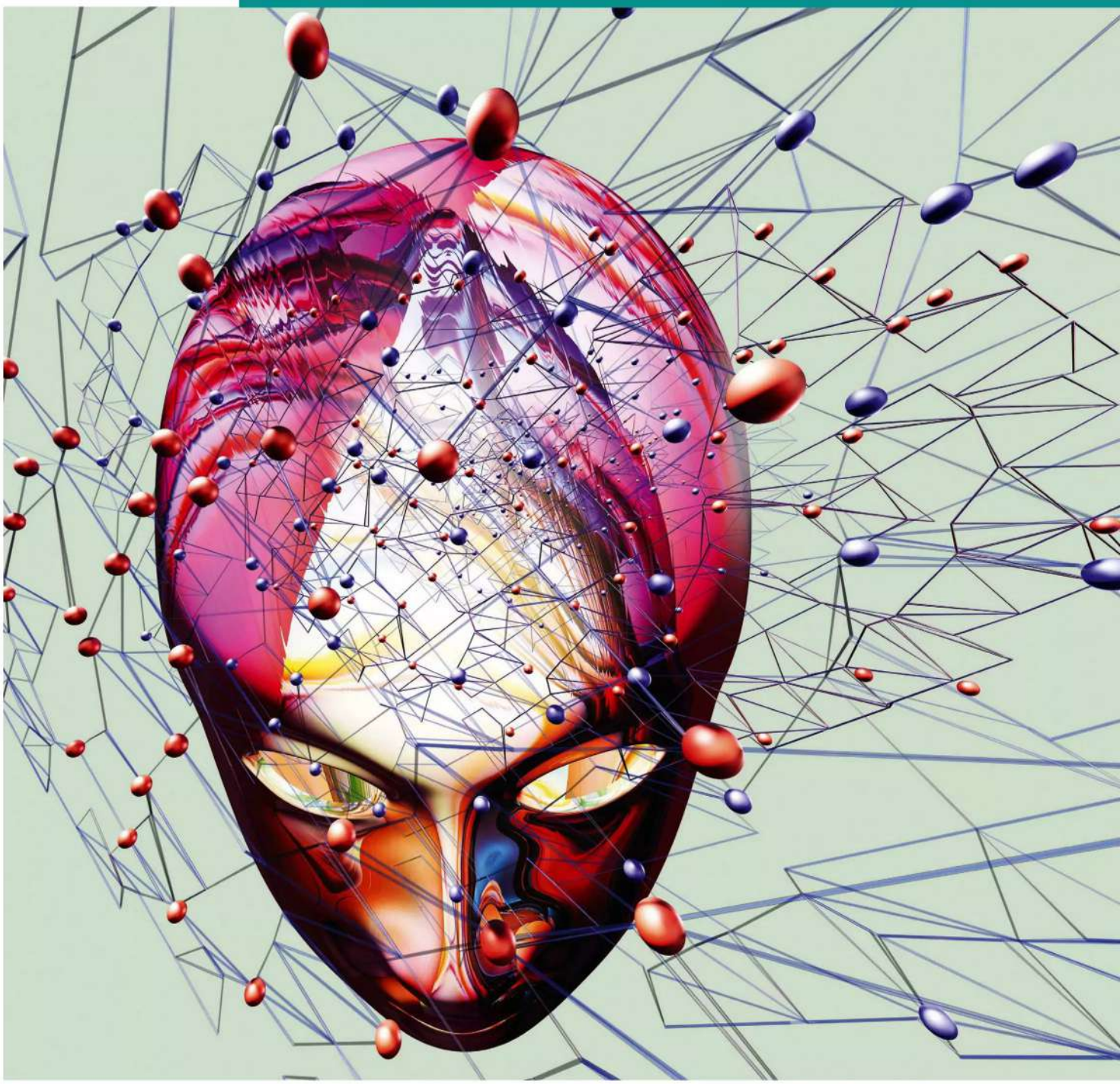
by **DR JULIA SHAW**

Julia is a research associate at University College London and the co-host of the Bad People *podcast on BBC Sounds. Her latest book is* Making Evil: The Science Behind Humanity's Dark Side *(£9.99, Canongate).*

Turn your Apple Watch into an alarm clock! p40

INNOVATIONS

PREPARE YOURSELF FOR TOMORROW



OTHER MIND-READING TECH

NEURALINK

Elon Musk's much-vaunted neurotech start-up requires implantable probes that work as a brain-computer interface. The actual technology remains secretive, but in April 2021 the company demonstrated a chimp using Neuralink to play a game of *Pong*.

OPENWATER

This start-up combines electro-optical technology, lasers and holographics to produce non-invasive imagery of the brain, as well as other organs or tumours, in incredible detail.

NEURAL DUST

Sometimes described as a Fitbit for the nervous system, neural dust refers to tiny implantable sensors that might pave the way for 'neuroceuticals'. These are diagnostic or therapeutic technologies that work by remotely activating dust-sized devices in the body.

NEUROSCIENCE

The injectable nanosensor that will one day read your thoughts

Mind-controlled machines, minus the wires-in-your-brain bit

A new kind of injectable biosensor might one day be able to read your thoughts or let you communicate using nothing but your mind.

Researchers at the University of California, Santa Cruz, have developed NeuroSWARM3. They say that its gold-plated nanosensors, which are the size of a single viral particle, could travel through the bloodstream and cross the blood-brain barrier. Once inside the brain they would act like a kind of antenna, turning neural activity into optical signals that could be wirelessly sent to an external device.

The researchers believe that in the shorter term it could help scientists better understand the mysteries of human cognition. Longer term, potential applications sound like the stuff of science fiction: composing messages with your thoughts, controlling exoskeletons with your mind, and doctors monitoring neurological disease with no invasive procedures.

"NeuroSWARM3 can convert the signals that accompany thoughts to remotely measurable signals for high-precision brain-machine interfacing," says Dr A Ali Yanik, who co-authored the research.

"THEY WOULD ACT LIKE A KIND OF ANTENNA, TURNING BRAIN ACTIVITY INTO OPTICAL SIGNALS"

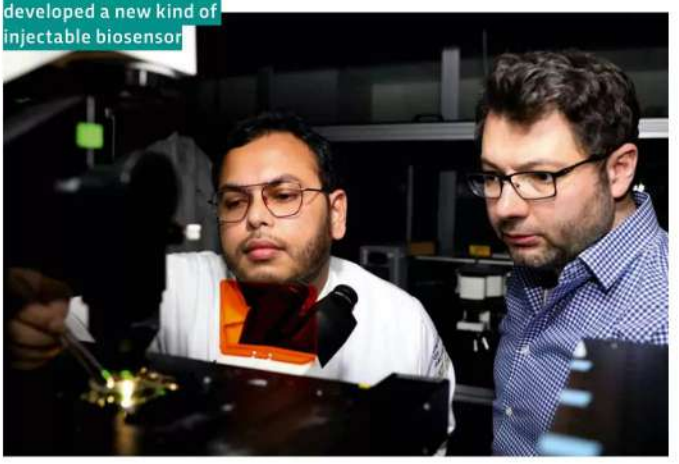
The technology works by tapping into the electrical signals that neurons use to send information to each other. This happens when humans do just about anything, including moving and thinking. NeuroSWARM3 is a new way to monitor that electrical activity and turn it into something a machine can read and interact with. In fact, Yanik's latest research shows that it's sensitive enough to pick up the activity of individual brain cells.

"The technology is similar to RFID," Yanik says. "With RFID, you have a back-scattering signal and then you read a static signal which delivers you the barcode or whatever it may be. In our case, we have this barcode, which is the electrophysiological signal of the cells, but it's not static and we are reading it wirelessly."

The fact that the technology operates at the nanoscale is what makes it incredible. Despite their tiny size, each nanosensor particle includes wireless power transfer, electronic translation of neural signals and broadcasting of those signals. And because the neurosensors can pass the blood-brain barrier, it means it can be injected directly into the bloodstream.

It's important to note that any testing on animals or humans has not yet occurred. If these experiments did take place, the procedure would be less invasive than comparable technologies such as Elon Musk's Neuralink. Whereas that requires a surgically implanted microchip and wires hanging out of the side of a person's skull, NeuroSWARM3 doesn't require surgery or implants or wires.

"We are just at the beginning stages of this novel technology, but I think we have a good foundation to build on," Yanik says. "Our next goal is to start experiments in animals."



Dr A Ali Yanik (right) has developed a new kind of injectable biosensor

GETTY IMAGES, C LAGATTUTA

INTERVIEW

Pegasus: the spyware that has set the world on edge

Pegasus software can hack a phone and access everything on it via a single phone call that doesn't even have to be answered. We asked Dr Tim Stevens, the head of the Cybersecurity Research Group at King's College London, to explain how it works and whether it can be stopped.

Last month, Amnesty International, working with over a dozen other news outlets, revealed that they had come into possession of a leaked list of politicians, journalists and activists whose phones had been hacked by a piece of spyware named Pegasus. The software was developed by an Israeli company called NSO Group, who said it has sold this technology to over 40 governments, although it won't reveal which ones. Pegasus can gather data, record videos and even take screenshots once it's on board, and requires only an unanswered phone call or a message to embed itself on to a device. The victims include the French president Emmanuel Macron and some 180 journalists from around the world.

PEGASUS HAS BEEN DESCRIBED AS THE MOST POWERFUL SPYWARE EVER, IS THAT ACCURATE?

It's hard to know whether it's the most powerful ever developed, because what else is out there? But I think it clearly has some functions that are a little more devious than we're used to seeing.

WHAT MAKES THIS DIFFERENT?

In the past, you might have been contacted via email, or some kind of social media messaging service, and asked to click on a link. Then when you click on the link, you download a piece of software onto your device and it'll do its work from there. What's remarkable about Pegasus is that it can get on your system without you clicking a thing. It's called a zero-click malware. All that needs to happen is for somebody to send a message to your device. It doesn't even need to be opened. It exploits flaws in the operating system of that device. We call these 'zero-day vulnerabilities' because they haven't yet been discovered by the vendor or by researchers. By the time it is discovered, they have zero time to patch it because they're only ever discovered when someone's used it to do bad things.

It is a fact that all very large pieces of software, like an operating system like Apple's iOS or Android or any other, including open source operating systems, have bugs. None of them are perfect. They present openings or opportunities for people to use to gain access. It's like locking up all the doors and windows, but leaving the kitchen window open overnight. If the burglar is going to recce the whole house, they will find it eventually, no matter how large your house. And that's exactly what goes on with software.

SO PEGASUS HAS A NUMBER OF WAYS OF GETTING ACCESS, AND IN SOME CASES IT'S AS SIMPLE AS A MESSAGE OR EVEN A PHONE CALL?

If you're a tech-savvy mobile phone user, alarm bells start ringing if you get a message that asks you to give a piece of software access to your address book or your email. If you decline that offer then you don't open that door. But with Pegasus you didn't even know the door was there.

Pegasus effectively jailbreaks your phone, it unlocks all this kind of administrative functionality that it then uses to position itself and hide itself and have access to everything that's going on in your phone. It's a very novel and impressive technical feat.

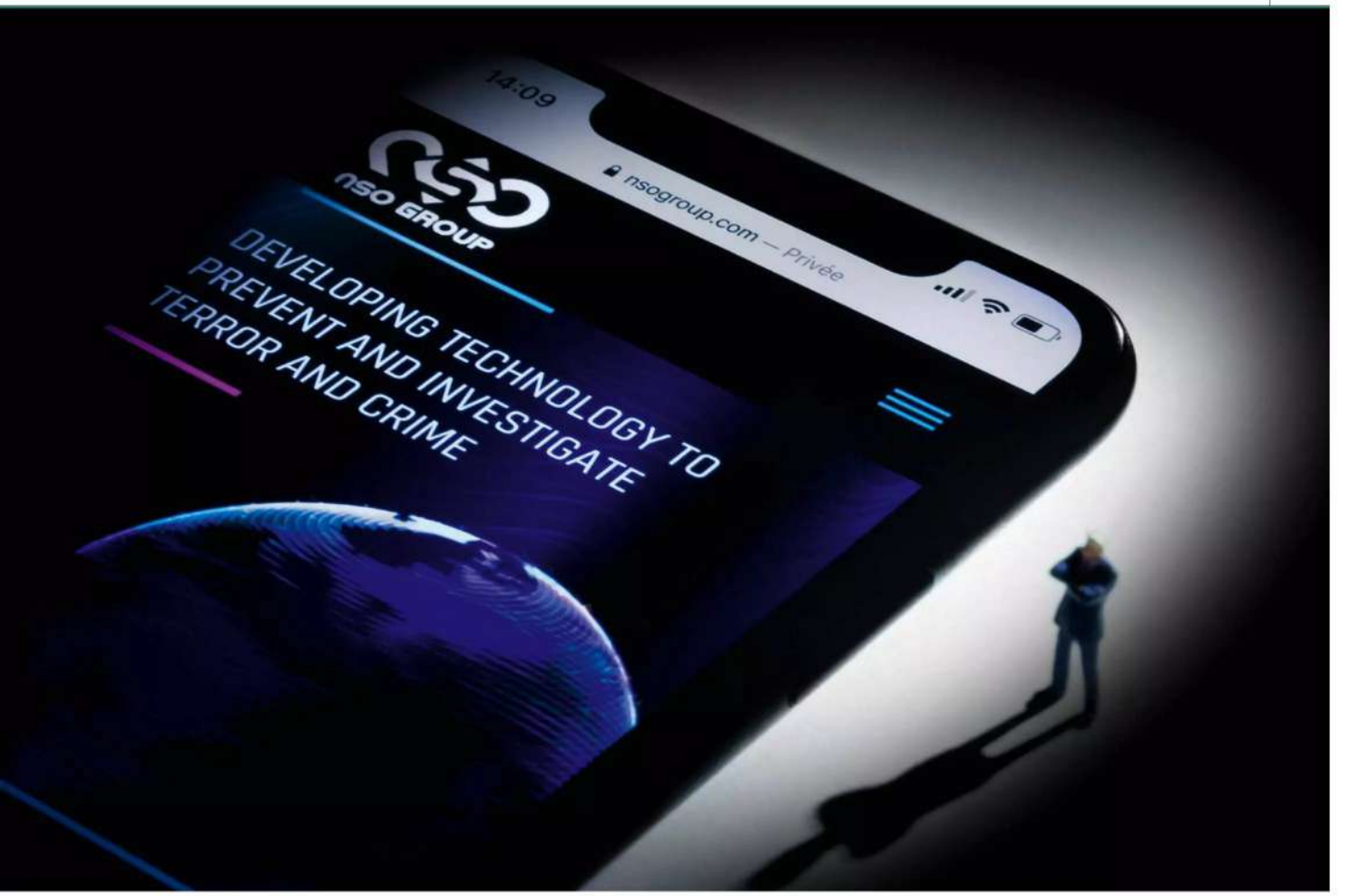
DO YOU HAVE TO PICK UP THE CALL FOR IT TO WORK?

No, there's always a digital handshake when you call someone. My device has to communicate with your device in some way. And when that connection is made you have a data link regardless of whether the other person picks up the phone. And that's the link that's being exploited by the zero-click pieces of software.

IS PEGASUS, AS A PIECE OF SOFTWARE, LEGAL?

It's a complex question. There are probably a few hundred answers to this, depending on what

GETTY IMAGES



country you're in. Most countries these days have legislation that says that you cannot use unauthorised access into a computer system, you simply can't do it. Essentially, you're not allowed to hack into a system.

There is no legislation that effectively and expressly forbids us doing that in a foreign country. It gets very complicated with mutual legal assistance treaties and extradition and so on. But essentially, there's no overarching international legislation that says that this stuff is illegal. And mostly that's because there's no overarching international legislation to say that espionage is illegal. And really, that's what we're talking about here.

WHAT CAN BE DONE ABOUT IT?

We first need to confirm who's been targeted. Disassemble phones and figure out whether Pegasus was there. I mean it's meant to be quite untraceable, but I believe that it leaves some digital tracks behind under certain circumstances. So it's a forensic issue at first.

After that it's a political or economic decision. What could these countries do? The NSO Group's clients in many cases are governments of countries. Are these governments going to admit to what they've done? Are they going to admit that they had contracts with the NSO – and if they do, you'd imagine they'd say that they were using it for law enforcement and counterterrorism. You know, I don't see that an honest answer to this will be particularly forthcoming, unless there's sufficient pressure from civil society and the press. I hope the press doesn't let this one go because it's shambolic behaviour.

↑ NSO's Pegasus spyware allows the remote surveillance of smartphones

GIVEN THAT A NUMBER OF JOURNALISTS SEEM TO BE ON THE TARGET LIST FOR THIS SOFTWARE, IT'S NOT A GREAT TIME TO BE A REPORTER, IS IT?

I think some deep-rooted cultural and political threads are running through public life at the moment that make being a journalist a slightly uncomfortable place to be. The bigger problem is that surveillance really only works when people internalise it. You want the watched to feel like they're being watched. Even if you're not watching them all the time. As long as people think they're being watched, they modify their behaviour. If journalists say, "I'm not going to have that conversation because my phone is on me," then that is a big concern.

Ideas we like...

↓ ...headphones that don't go on your head

What if putting on music didn't have to mean shutting yourself off from the world? Sony's new Neckband Speaker gives your ears a rest and sits on your shoulders, firing your audio towards your ears in a focused beam. There's a built-in microphone and Bluetooth connectivity, which means you can take calls or listen to music up to 30m away from your computer – no more excusing yourself from a meeting to make a cup of tea. You also needn't worry about disturbing your partner or housemates, as Sony claims the upward angle of the full-range speaker optimises sound for your ears only. Though we'd have test that one for ourselves to believe it! Weighing only 113g, the neckband is light and comfortable. Take your pick from charcoal grey or pristine white. Can we see it in rose gold?

Sony SRS-NB10
£135, sony.co.uk

↑ ....a multisensory movie experience

The new FLEXOUND Pulse chair brings a whole new sense to your cinema experience: touch. The latest horror movie could literally shake you to your core, while the orchestral opening of the next Marvel film will make the hairs stand up on your neck. Instead of a loudspeaker blaring a film's audio at you, the Pulse uses speakers built into the chair to deliver sound that you can feel. The system offers all the intense sound you'd expect in a cinema, except now you can also feel frequencies of up to 1,000Hz on your skin.

Currently, the chair concept is only available for cinemas, but it's ready to be licensed to a furniture manufacturer willing to put their body where the sound is. FLEXOUND even mentions a future with car brands, creating personal 'sound zones' for every passenger or making quiet electric vehicles sound like they have eight-cylinder engines.

FLEXOUND Pulse
flexound.com

→ ...a snowglobe for your Apple Watch

Not all tech needs to come with wires and buttons. This NightWatch orb magnifies an Apple Watch's display to effectively turn it into an alarm clock for your bedside table. There's a slot in the back that holds the watch's MagSafe charger, and tapping the surface of the orb will wake up the watch screen so you can see the time. Plus, the shape of the NightWatch amplifies sound to transform your watch into an effective alarm clock.

NightWatch
£45, nightwatch.shop

←

...a TV that rolls down when you're done

When you turn this TV off, the display just rolls itself up, and tucks into the small speaker cabinet below. Alternatively in 'Line View' mode, it shrinks down to about a fifth of its height to work as a display for the integrated sound bar. It's an achingly cool party trick that's made possible by OLED technology. This kind of display doesn't require backlights – the OLED crystals generate their own light when a current is passed through them. This means they can, if manufactured in a certain way, be built into a flexible screens. We've seen demos of this bendable screen technology for a couple of years now, but manufacturing is still fairly expensive and hard to perfect, which goes some way to explaining why you'll have to cough up a house deposit to own one of these TVs...

LG OLED RX
£99,999, lg.com

↑

...a smart-looking gaming laptop

Most gaming laptops wouldn't look out of place in a steampunk rave with all the extra wings, gubbins and lights that get bolted on to the design, which is why this understated powerhouse from Gigabyte appeals to us. It's a punchy computer in a relatively slim, sleek case. The Aorus is powered by the latest Nvidia SUPER graphics card, which is developed to handle complex lighting graphics used in the latest games. The display can run at a blistering 300Hz, which means games will look incredibly smooth on-screen. If you're one of the gaming pros this laptop was designed for, that rapid refresh rate means that there's no discernible delay between your input and what happens on screen. And of course, the laptop comes with a true mechanical keyboard to provide satisfying clicks with each key press. If you need help justifying the outlay, we're told all this machinery means it's pretty adept if you need to do a bit of video or audio editing.

Gigabyte Aorus 17G
From £1,599, gigabyte.com

↓

...a speaker that disappears into the decor

We're rather besotted with these unconventional Wi-Fi speakers borne out of a collaboration between Sonos and Ikea. The flat panel speaker is about as thick as a flatscreen TV and can be mounted flush against a wall or stood up on a shelf using the kickstand. Ikea offers interchangeable front panels so you can shake things up when you tire of its looks. There are controls on the side but the speakers also work with Sonos's S2 app, which means you can send music seamlessly to different parts of your home, and access the full range of streaming services that plug into it.

Symfonisk Picture Frame Wi-Fi Speaker
£179, ikea.com

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TRULY EGG CELLENT

SO MUCH OF LIFE ON EARTH STARTS WITH AN EGG. IT'S AN INCREDIBLE PIECE OF BIOLOGICAL DESIGN THAT GOES BEYOND THE FAMILIAR. HERE'S A CELEBRATION OF THE INCREDIBLE WAYS EVOLUTION HAS FOUND TO KICK-START LIFE...

WORDS: JULES HOWARD

EGG EMOJI

"What looks like a mouth is actually a fracture-line that runs along the top of the egg," says shield bug expert Maria Justamond, commenting on this cluster of emoji-like insect eggs on the underside of a leaf. "When the baby shield bug is ready to emerge, the egg opens up like a trapdoor."

More than 99 per cent of all animals that have ever lived on planet Earth have, in the first moments of life, hatched from an egg. Yet for all their abundance, eggs continue to amaze scientists with their unique adaptations and mind-blowing evolutionary workarounds.

"I've always had a bit of a soft spot for their eggs," Justamond adds. "I love how varied they are in colour and size, and how each shield bug species has its own interesting life cycle."

PAUL BERTNER/MINDEN PICTURES

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UNHATCHED AND UNDERCOVER

Unhatched stick insects regularly come under attack from parasitic wasps, whose predatory larvae ransack their eggs and eat everything inside. To counter this threat, some species of stick insect have evolved eggs that look like seeds. Each egg has a handle-like structure full of oil, called a capitulum, that mimics a similar structure in some plant seeds. This entices hungry ants who, thinking the eggs are food, take them back to their nests for safe-keeping. Deep within the nest colony, the stick insect eggs continue their development safe from marauding wasps.

This is one of many ingenious stick insect egg innovations. Some species have eggs so tough they can pass through the guts of seed-eating birds, for instance, and one species even has eggs that can float in seawater.

"Insects eggs are just as subject to natural selection and evolution as any other stage," says Prof Adam Hart, entomologist and BBC broadcaster. "They really are quite remarkable once you start looking at them."

→

EGGS-TREMELY BUOYANT

Covered in tiny finger-like projections, the eggs of some mosquito species bind tightly against one another when laid, forming a little raft of eggs that floats on the water surface. Special proteins on the surface of each egg actively repel water, causing the raft to curve upwards at its outermost edges. This helps the egg-raft stay afloat, should choppier conditions occur.

Because mosquitoes transmit a host of life-threatening diseases, many scientists are interested in the egg-laying behaviours of female mosquitoes and how they might be curbed. In 2019, a team of scientists from the University of Arizona managed to turn off a single gene (known as Eggshell Organising Factor 1), which affects the proteins that provide waterproofing to the developing egg. The result? A life raft that takes on too much water, eventually sinking and killing all the unhatched mosquitoes on board.

PIOTR NASKRECKI/MINDEN PICTURES X2, INGO ARNDT/MINDEN PICTURES

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DAD OF THE YEAR

With some species as large as a human palm, the giant water bug is a voracious wetland predator. Yet throughout the breeding season, males show a softer side. During mating, the female lays eggs on the male's back, which are guarded until they hatch. Relieved of her duty, she moves off elsewhere to mate again.

Far from being undone by the labours of childcare, males actually benefit from this unusual relationship. In 2016, through a series of experiments, scientists discovered that females actively seek out males with the eggs of other females upon them. Like a peacock's tail, a back bejewelled with eggs is all about turning heads.

But why has parental care evolved at all in these giant bugs? "There's likely to be something about these bug eggs that makes them very worth protecting, such as being large, expensive to produce and susceptible to attack from parasitic wasps," says Dr Gavin Broad, the Natural History Museum's curator of insects.

LOOKING SWELL!

Lit from behind, the contents of this shark eggcase are clear to see. A young swell shark with yolk sac, still weeks from emerging, is taking shape. Its tail lashes repeatedly from side-to-side, flushing water around the eggcase to maintain a healthy flow of oxygen.

The eggs of sharks and rays differ from the eggs of bony fish. Most are endowed with long tendrils, which can be wrapped around vegetation, and the case is often rectangular, resembling ravioli. The covering is extra strong, courtesy of collagen, which is a structural protein also found in human bones, tendons and ligaments. As well as deterring predators, this collagen-heavy suit of armour helps keep the egg from decaying, meaning that some eggcases can house a developing embryo for up to 12 months.

After a young shark or ray hatches, many eggcases wash up on shorelines where beachcombers greet them with the colloquial name, 'mermaid's purse'.

↑

DON'T MESS WITH MOTHER

A female Pacific octopus protects her brood of 50,000 eggs, which dangle from the roof of an undersea cave. Every individual egg, each the size of a grain of rice, has been collected by the octopus and hung carefully on threads to create something not dissimilar to a beaded curtain.

Through day and night, she carefully removes algae and parasites from her eggs, while pumping water across the strands to maintain a steady flow of oxygenated water to help the eggs grow. So protective is the female of her unhatched offspring that she foregoes hunting completely, instead relying on energy reserves gathered over her five-year lifespan. The effort will eventually kill her, but the strategy works for octopuses. In life's lottery, it can pay to invest everything that you have on tickets. Particularly if you have a deep, dark cave within which those tickets can be kept safe.

RALPH PACE/MINDEN PICTURES; FRED BAVENDAM/MINDEN PICTURES X2

SEA OF SPAWN

Synchronising with the tides and the Moon's cycle, corals of numerous species, such as this staghorn coral, release millions of eggs and sperm into the water all at once. By mass-spawning together, corals provide predators temporarily with more food than they can possibly eat, thereby enhancing the chances of at least some of their offspring surviving.

But coral mass-spawning events are not what they once were. Catastrophic declines in coral populations, caused by climate change and reef diseases, have occurred across the world, so much so that the fate of some coral species rests on captive populations kept in aquarium tanks. By maintaining the genetic diversity of these captive colonies, it's hoped that some reefs can be replanted with disease-resistant strains of coral that are more resilient to the problems that humans are causing.

↑

TAKE THE PLUNGE

Hiding beneath a leaf, a tiny male glass frog guards its fledging tadpoles, as they drip from out of their jelly-like eggs into the waters below. Unlike most frogs, this species produces only a handful of eggs at a time, which it protects for as long as possible. The glass frog's body is translucent, an adaptation that softens the amphibian's edges, making it harder for predators to see.

"I can confirm it's a highly effective strategy," says Lucy Cooke, zoologist and patron of Amphibian and Reptile Conservation, who once joined a search party for the tiny amphibians in a remote Colombian wetland. Alas, they were unsuccessful. "Glass frogs and their eggs merge into whatever they're sitting on," she explains. "It was only the sound of their amorous peeps that gave them away."

by **JULES HOWARD** *(@juleslhoward)*
Jules is a zoologist and author. His latest book is Encyclopedia Of Insects *(£14.99, Wide Eyed Editions).*

→

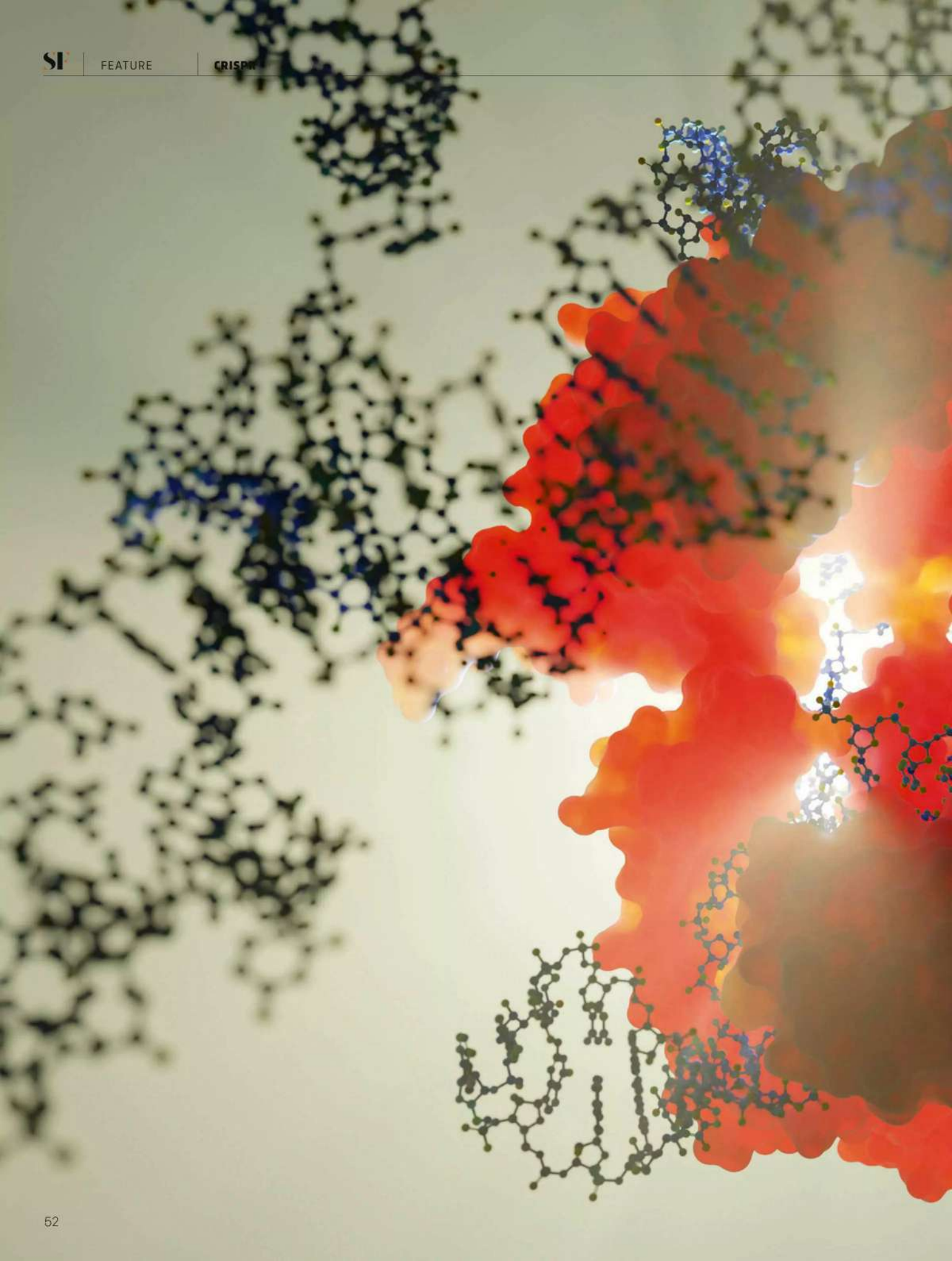
STICK TOGETHER

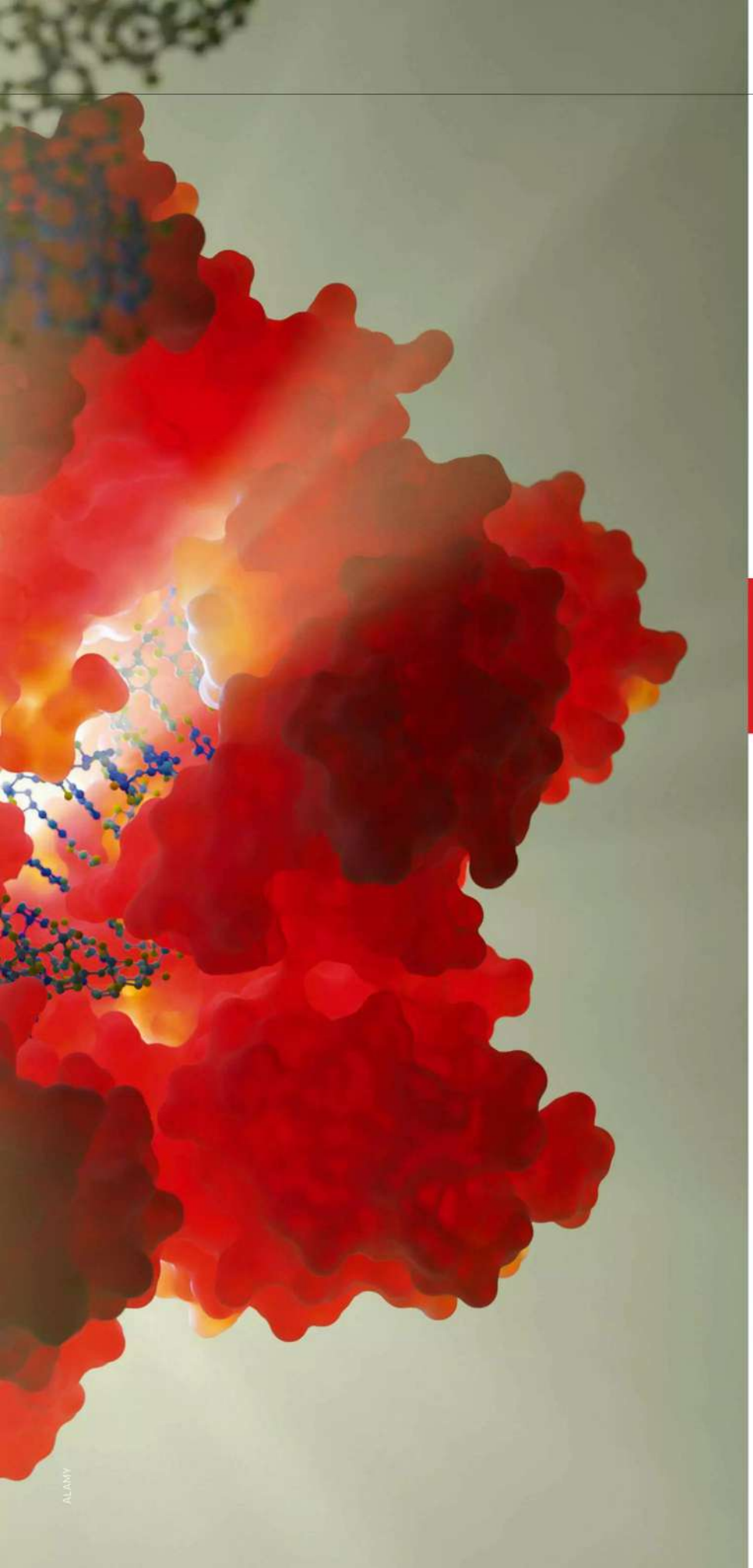
Row upon row of baby clingfish develop, each within its own biosphere. Yet look closely and you'll see a familiar evolutionary innovation: yolk, the yellow blobs within each egg.

Yolk contains vitamins, fats and minerals – all that life needs to sustain a growing embryo. But the familiar yellow colour of yolk comes from something else entirely: carotenoids, which are naturally occurring pigments found throughout the animal kingdom.

What do these carotenoids do? The best theory is that the yellowy pigment is thought to play a role in 'taming' rogue oxygen atoms (known as free radicals) that rampage through cells and damage molecules, including DNA. In newly developing embryos, where every cell division counts, the effects of free radicals may be especially harmful, hence the near-universality of carotenoids in eggs laid throughout the natural world. **SF**

PETE OXFORD/MINDEN PICTURES, NICO VAN KAPPEL/BUITEN BEELD/MINDEN PICTURES





ALAMY

A REVOLUTION IN THE MAKING

Scientists will soon have the tools to rewrite the book of life, and in doing so, edit out sections that cause disease, piece by piece. But is the technology safe and will all of us get the benefits, or will it be the preserve of those who can afford it?

WORDS: IAN TAYLOR

Scientists are a cautious bunch, fond of a caveat even when describing their own research. "Our favourite expressions are 'Yes, but...' and 'On the other hand...' and 'It remains unclear...'" says gene editor Dr Fyodor Urnov. "So please add all of that to what I'm about to say. If CRISPR realises 10 per cent of what we practitioners of gene editing dream it to be able to do, it will rival the greatest advances in the history of biomedicine as a technology to impact public health."

Urnov is talking via a crackly Zoom link from his office at the Innovative Genomics Institute (IGI) in Berkeley, California, which is at the forefront of what may prove to be the defining scientific breakthrough of the 21st Century.

CRISPR is a genome editing technology that allows scientists to cut DNA with incredible precision and insert or delete DNA to correct unwanted mutations. To oversimplify the technology, it's the power to edit the building blocks of life, just like text on a computer screen. Not only could it enable scientists to switch off genes that lead to a broad spectrum of disease, but it will unshackle all of us from the genetics we're born with.

"The knowledge gained is amazing and it's just really accelerated basic research.

Jennifer Doudna, who collaborated with Emmanuelle Charpentier on the development of CRISPR and founded the Innovative Genomics Institute

SHOULD ALTERED DNA BE PASSED ON TO THE NEXT GENERATION?

By targeting 'germline' cells in a given individual, any edits made would be passed down to that person's children and future generations beyond. This raises enormous ethical questions about what edits are made and why, with natural comparisons to eugenics.

BELOW The Innovative Genomics Institute in California

That in itself is already transformative," says Dr Robin Lovell-Badge, from the Crick Institute. "And the notion that we can actually treat people with genetic diseases in a way that was never possible before is mind boggling."

For much of the past decade, the technology has been confined to the lab. Now, though, the first CRISPR therapies are changing the fate of people born with debilitating inherited conditions. Most of us haven't realised it yet, but we're in the foothills of a profound medical and technological revolution that raises not only the prospect of new treatments and cures, but also huge questions about ethics, equality and health justice.

The incoming wave of gene-editing applications has been compared to the Industrial Revolution or the birth of the internet in terms of the game-changing impact it will have on society.

IGI, UC BERKELEY

BIG CLAIMS

Biochemist Dr Jennifer Doudna established the IGI to tackle all of that and more. As a non-profit organisation, the institute exists not just to research gene editing, but also make it affordable and accessible to everyone. It's a big claim, given the breadth of CRISPR's potential, so the IGI's leadership team agreed to give *BBC Science Focus* an exclusive overview of its efforts.

It was there on the Berkeley campus where Doudna and Dr Emmanuelle Charpentier changed the world nearly a decade ago. Their collaboration led to the development of CRISPR-Cas9, the gene-editing tool described in a landmark 2012 paper that won a Nobel Prize.

CRISPR 101

An oversimplified guide to a medical revolution

WHAT IS CRISPR-CAS9?

A means of editing our DNA, and that of any living thing. It's adapted from clever DNA sequences found in bacteria and archaea, which 'snip' a piece of DNA from invading viruses, so they can better repel them in the future.

HOW DOES IT WORK?

Think of the Cas9 enzyme as a pair of genetic scissors that allows scientists to cut a double strand of DNA at a precise location on a given genome. When the cut is made, it gives us the opportunity to either delete a section of DNA or add a new section. It's the power to remove unwanted DNA or insert beneficial genetic information.

WHAT WILL IT DO?

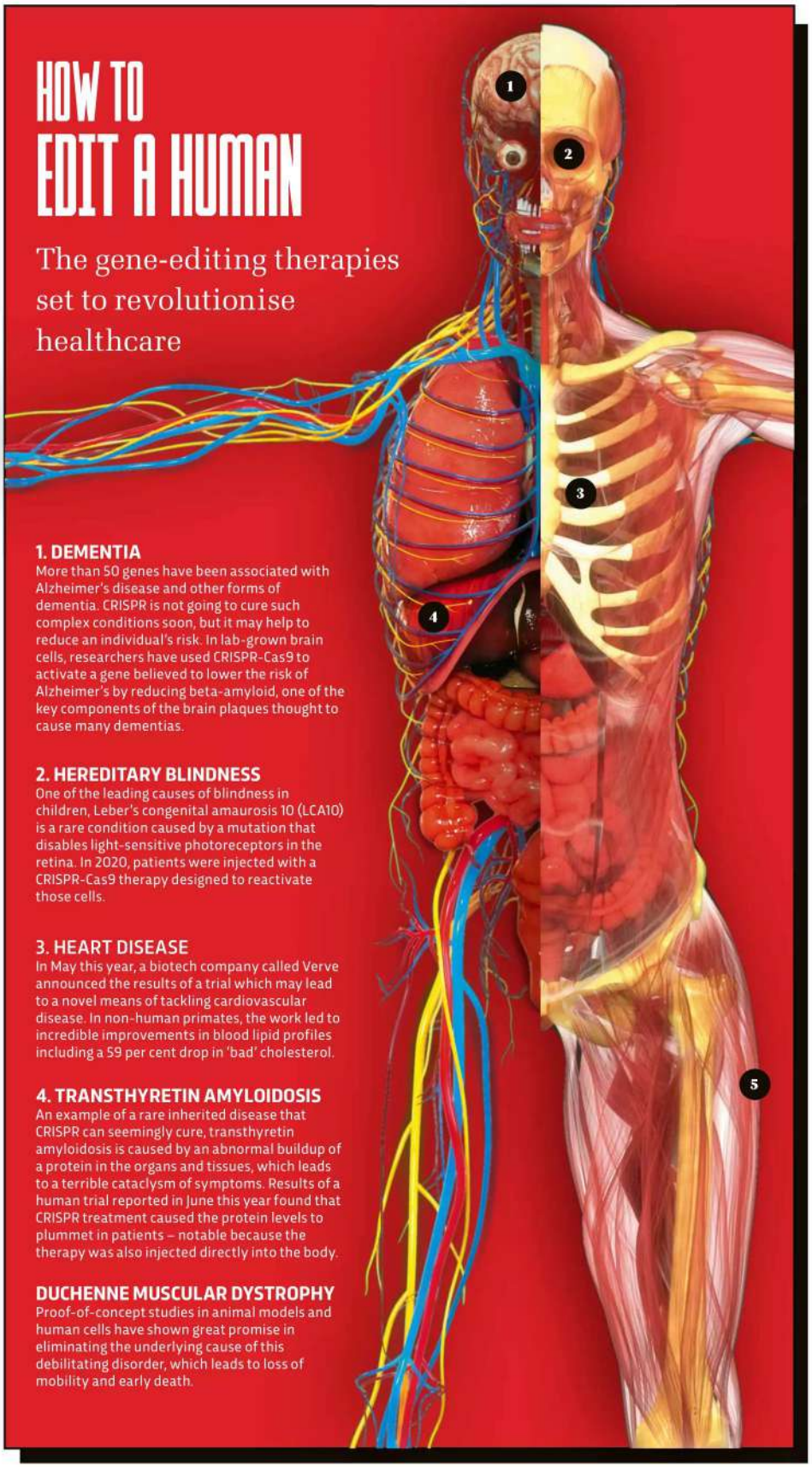
The ability to edit DNA sequences is effectively the power to rewrite the source code of life itself. In theory, it offers a powerful means of 'switching off' the DNA responsible for any inherited disease. It could also be used as a therapy to introduce genetic advantages that may reduce a person's risk of a given condition. Likewise, it could be used to reduce the threat of diseases such as malaria by editing the genomes of the mosquitoes that carry the infection.

WHAT ABOUT BEYOND HEALTH?

One of the (many) debates around the technology is about treatment versus 'enhancement'. If CRISPR can be used to target DNA associated with disease or good health, then it could also be used to affect DNA responsible for physical traits or abilities.

HOW TO EDIT A HUMAN

The gene-editing therapies set to revolutionise healthcare



1. DEMENTIA
More than 50 genes have been associated with Alzheimer's disease and other forms of dementia. CRISPR is not going to cure such complex conditions soon, but it may help to reduce an individual's risk. In lab-grown brain cells, researchers have used CRISPR-Cas9 to activate a gene believed to lower the risk of Alzheimer's by reducing beta-amyloid, one of the key components of the brain plaques thought to cause many dementias.

2. HEREDITARY BLINDNESS
One of the leading causes of blindness in children, Leber's congenital amaurosis 10 (LCA10) is a rare condition caused by a mutation that disables light-sensitive photoreceptors in the retina. In 2020, patients were injected with a CRISPR-Cas9 therapy designed to reactivate those cells.

3. HEART DISEASE
In May this year, a biotech company called Verve announced the results of a trial which may lead to a novel means of tackling cardiovascular disease. In non-human primates, the work led to incredible improvements in blood lipid profiles including a 59 per cent drop in 'bad' cholesterol.

4. TRANSTHYRETIN AMYLOIDOSIS
An example of a rare inherited disease that CRISPR can seemingly cure, transthyretin amyloidosis is caused by an abnormal buildup of a protein in the organs and tissues, which leads to a terrible cataclysm of symptoms. Results of a human trial reported in June this year found that CRISPR treatment caused the protein levels to plummet in patients – notable because the therapy was also injected directly into the body.

DUCHENNE MUSCULAR DYSTROPHY
Proof-of-concept studies in animal models and human cells have shown great promise in eliminating the underlying cause of this debilitating disorder, which leads to loss of mobility and early death.

"I think we both had a little sense of, you know, kind of a chill," she says. "I still remember that feeling of hairs standing up on my neck, thinking there's something really interesting here. And I would wager that neither of us at the time had any idea where it would end up, because I don't think one ever does."

CRISPR isn't the only gene-editing technology, and the IGI is not the only institute pioneering the field of study. But CRISPR is more versatile, easier to use and cheaper than a lot of other technologies. And what's astonishing is the speed of progress. In less than a decade it's gone from discovery to human trials and potential cures, something that's practically unheard of in biomedicine.

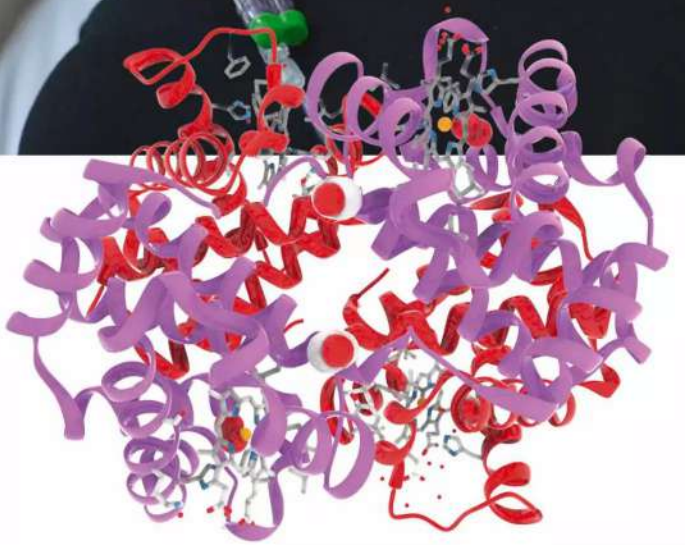
"It's a little bit of whiplash," says Dr Brad Ringeisen, executive director of the IGI. "Think about nanoparticles, the nano revolution. Pfizer has nanoparticles in their COVID mRNA vaccine, but that [technology] has taken 30 or 40 years."

FIRST SUCCESSES

People born with sickle cell disease will be among the first to benefit from advances in gene editing. In 2019, a woman called Victoria Gray became one of the first people in the world to be treated for a genetically inherited disease with a CRISPR-based therapy. Born with sickle cell anaemia, she required strong pain medication and regular blood transfusions to stave off the effects of the mutated gene that makes red blood cells warp and block the flow of blood and oxygen around the body. Aside from bouts of excruciating pain, sickle cell anaemia can lead to stroke, hypertension, organ damage and more.

The treatment was not simple. Doctors removed bone marrow cells from Gray and the other patients in the trial, then used CRISPR to edit a gene that activates production of foetal haemoglobin, a protein that can alleviate the symptoms of sickle cell disease. The patients then underwent chemotherapy to destroy most of their bone marrow, after which billions of edited cells were infused back into their bodies.

GETTY IMAGES X2, SCIENCE PHOTO LIBRARY, SARAH CANNON RESEARCH INSTITUTE



WOULD YOU CRISPR YOUR KIDS?

If a child is born with a genetic mutation that causes disease, pain or a shortened lifespan, most parents would be receptive to treatments that nullify that mutation. What about other edits? Would you choose your kid's eye colour or personality traits if you could? Or if you knew that your child's classmates were edited to maximise certain cognitive abilities, would you follow suit so your child is not left behind?

ABOVE and LEFT Victoria Gray, who volunteered to have her sickle cell anaemia treated with CRISPR-based therapy. To carry out the treatment, CRISPR was used to edit a gene that activates foetal haemoglobin (left), a protein that can alleviate sickle cell anaemia

ABOVE RIGHT Sickle cell disease causes the body to produce unusually shaped red blood cells. These cells do not live as long as other red blood cells and can block blood vessels, leading to problems

Gray no longer requires medication or transfusions, and neither do the other people in her trial, which included patients with a related blood disorder. It seems that a one-time CRISPR treatment has cured them.

"Sickle cell disease is probably the easiest target that affects the most people," says Ringeisen. "It's about as simple as you can possibly get: you go in and either turn on an alternative gene or you try to correct the one thing. One hundred thousand people in United States have sickle cell disease and I think it's over a million people worldwide. So there's a huge impact that can be had."

The IGI is preparing its own sickle cell trial, but the institute's scope also includes many other conditions. As well as blood disorders, it has active research projects on autoimmune disease, neurological disease, cancer and COVID-19. One promising avenue of research is with T-cells, sometimes described as the troops on the ground of our immune system.

Dr Alex Marson, the IGI's director of human health, is running a lab that is working to engineer T-cells using CRISPR to treat different kinds of disease. He is currently planning a clinical trial with a family where a strong genetic mutation has caused different manifestations of autoimmune disease in the younger generation.

"In the lab we've corrected cells from these children," he says. "Now we're working towards doing a clinical trial to take those gene-corrected T-cells and infuse them into at least one of these young adults to try to restore balance in the system and treat the autoimmune disease."

Whereas current T-cell therapies are wildly expensive, Marson envisions ▶

SHOULD 'BOUTIQUE' THERAPIES BE APPROVED?

The good news: a gene-editing therapy is invented that effectively cures an inherited disease. The bad news: it costs more than £2m per dose. Should regulators approve that therapy, on the basis that it saves lives? Or oppose it because less than 1 per cent of people can afford it and it could lead to a 'gene gap', where the wealthy have the ability to make themselves 'better' than everyone else?

a future where off-the-shelf T-cells are manufactured to treat different kinds of disease, their production industrialised to a scale that makes them accessible to anybody who needs them.

"We can treat infectious diseases by designing immune cells that recognise infections," he says. "I think we're going to have this sort of flexible ability to actually write the language of the DNA in the immune cell and use it in a drug platform."

This is where things start getting really interesting, because it showcases just how broad the medical applications of CRISPR will be. Its potential lies not just in those conditions caused by a single genetic mutation like sickle cell disease, but any disease that has a genetic component, either in terms of susceptibility or protection. That includes many of the major killers, including cancer, cardiovascular disease and neurodegenerative disease, plus chronic conditions like inflammatory bowel disease and rheumatoid arthritis.

"All disease is on the map," says Ringeisen.

DISEASE PREVENTION

Part of what gives scientists optimism is that gene editing can be used to bestow protective DNA on a person as well as correcting unwanted mutations.

"We know there is a genetic change you can make that will dramatically lower your risk of heart disease," says Urnov. "How do we know that? Because of very rare individuals who have those genetic changes. And when you study lots of them, it's kind of jaw-dropping. I'm not going to say they're immune to heart disease, but they're close to it."

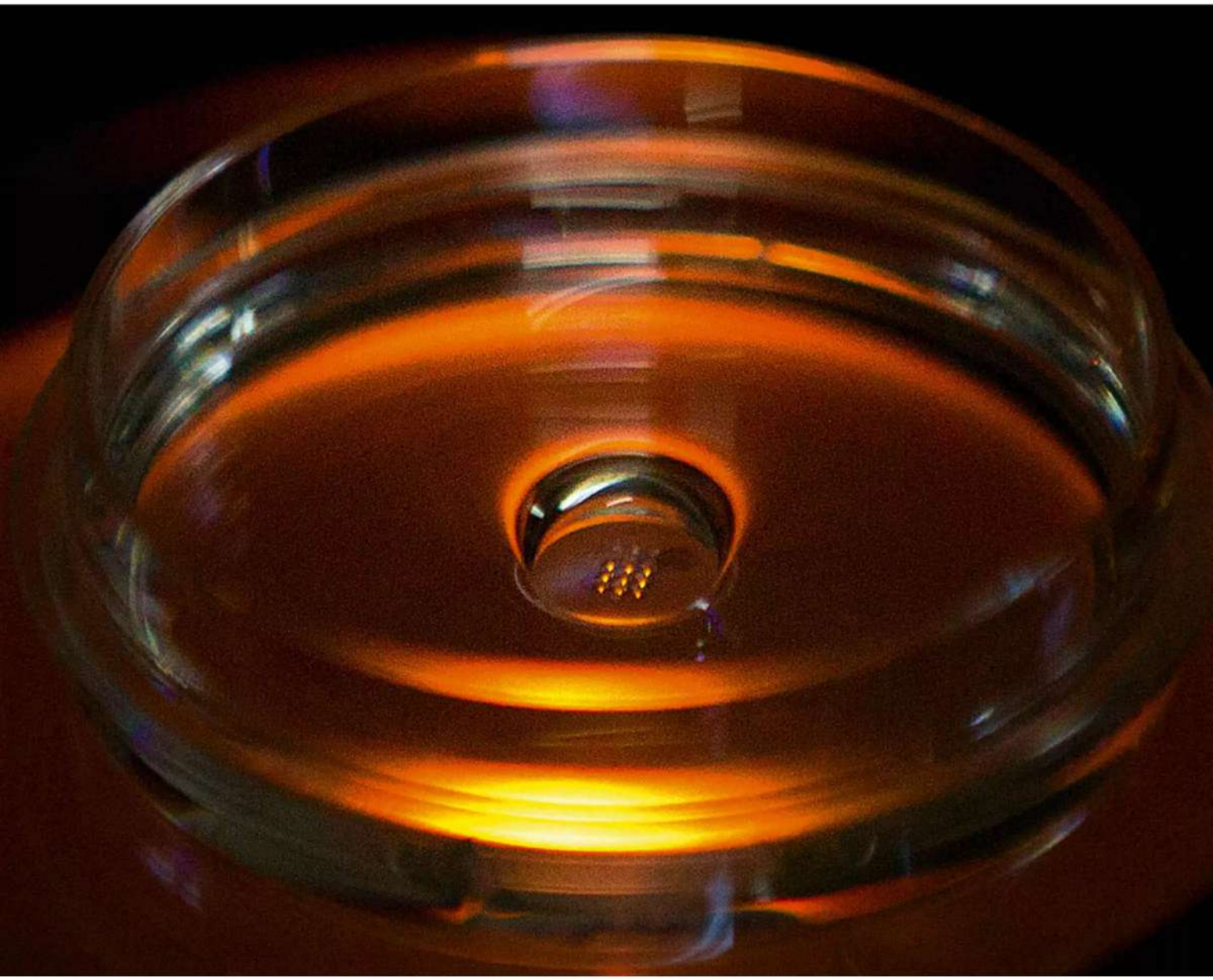
Doudna believes that CRISPR could even be used more to prevent disease than to treat it. "Imagine a time when people get their genome sequenced and be told that you have a gene that makes you have a higher likelihood of getting cardiovascular disease," she says. "But you have the option of editing your cells so that you don't have to wait to find out if you're one of the unlucky folks that is susceptible."

Today, lots of us take preventative action to protect our future health. It could be anything from eating a high-fibre diet to keep heart disease at bay, to having a double mastectomy because breast cancer runs in the family. Would you be comfortable editing your DNA to achieve the same results? It's harder to do the cost-benefit analysis when you're talking about such experimental therapies. There are some who will say that any form of gene editing is 'playing God' and conspiracy theories around COVID-19 vaccines show how mistrust in new technologies can spread.

"There can be misrepresentations or just misconceptions embedded in the public mindset that can have a negative effect on what I think should be positive advances," Doudna says. "Another example of that is the whole anti-GMO movement."

In November 2018, twin girls were born in China, the so-called CRISPR babies. Biophysicist Dr He Jiankui announced that he had created the world's first genome-edited babies to widespread condemnation. He engineered mutations in human embryos that were later implanted into a woman, crossing an ethical boundary by altering the human germline,

BELOW Emmanuelle Charpentier, who worked with Jennifer Doudna on the development of CRISPR



meaning the edits he made would also be passed on to future generations. Additionally, he was criticised for flouting normal safety procedures.

Jiankui claimed that he had disabled a gene called CCR5, offering protection against HIV. His critics pointed out that he could have also inadvertently caused mutations in other parts of the genome. Jiankui was jailed in China for three years at the beginning of 2020 and ordered to pay a three million yuan fine, his work a stark warning to everyone in the gene-editing world.

"This field is experimental and we are one 'severe adverse event' from the entire effort being frozen," Urnov says. "The painful thing for me and for tens of thousands of folks like me who have spent 40 years building human genetic engineering to treat disease, you know, this technology's now tainted with the concept of designer babies.

"We have 250 million people on planet Earth with genetic disease. We should not be talking about designing anyone. We should be putting all of our attention to the fact that there are hundreds of millions of our fellow human beings that have had their fate handed to them on genetic platter," he adds.

There are other challenges to overcome, too. One of the major criticisms of Jiankui's work stems from the fact that gene editing is not yet so precise that scientists have ●

ABOVE A microplate containing embryos that have been injected with Cas9 protein in a laboratory in Shenzhen, China

UC BERKELEY, SHUTTERSTOCK

absolute faith that any edit only affects the part of the genome being targeted. There can be so-called 'off-target' effects: unintended genetic modification that occurs elsewhere on the target genome. A worst-case scenario in clinical terms might be 'genotoxicity', where an off-target effect causes DNA damage that could lead to cancer.

For this reason, what's known as the 'delivery challenge' of CRISPR is a major focus of research, both at the IGI and beyond.

"We can only gain confidence in the safety of these procedures by performing clinical trials," says Dr Ross Wilson, the IGI's director of therapeutic delivery. "We are not so hubristic to think that we have the ability to forecast every possible outcome when a new therapeutic procedure is attempted, which is why these trials are being performed methodically and without haste. Once we have confidence that people's lives are being saved or transformed for the better, without incurring unwanted outcomes, the technology can be moved into other applications, reducing risks of heart disease, for example."

There are ways to offset this risk of unintended consequences of gene editing. A patient's own cells can be sent to the lab for 'trial editing', giving an informed look at what is likely to happen inside that patient's body when they are dosed.

CRISPRoff technology is also under development. This tool allows researchers to target the epigenome, rather than the genome itself. That is, scientists can turn off a particular gene without cutting a strand of DNA by instead targeting the proteins and other molecules that attach themselves to DNA and control when that gene is switched on or off. Because the genome itself is untouched, researchers expect the risk of unwanted effects to be lower.

"The pandemic taught us that the public has a major craving for things to be declared 'safe' or 'unsafe', but in reality it's all about the balance between risk and benefit," says Wilson. "That ratio looks extremely promising for CRISPR technology, and it improves each year, so the future is bright for therapeutic genome editing."

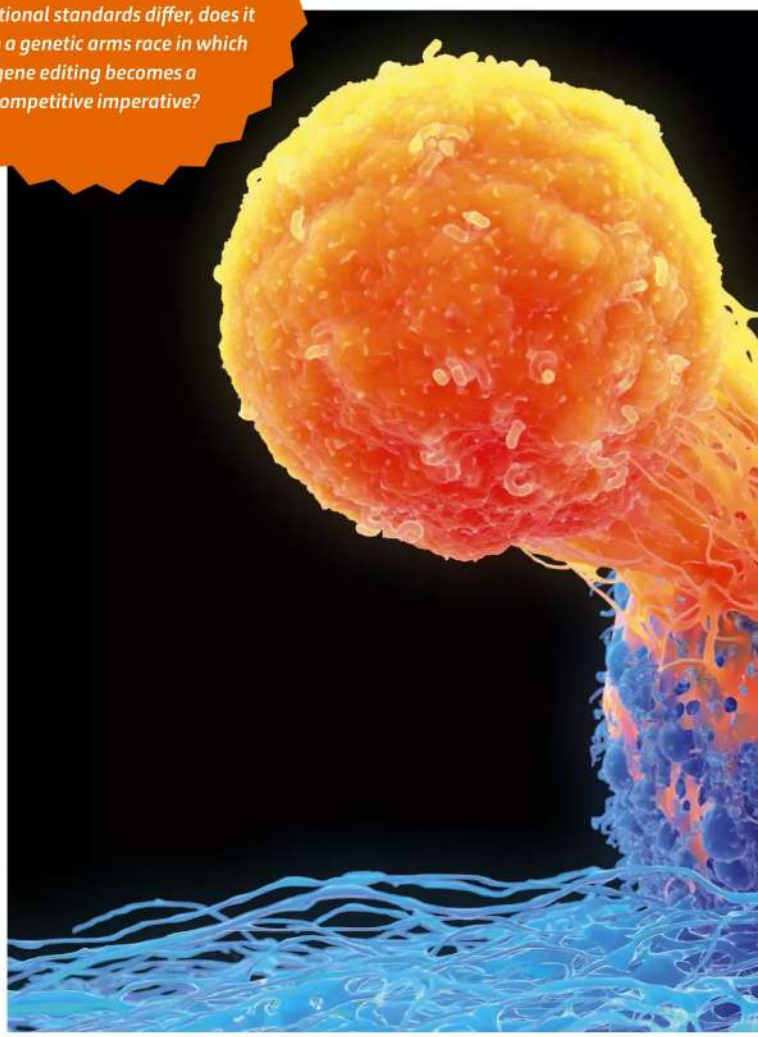
HEALTH INEQUALITY

Doudna's dream for CRISPR is to make it "the standard of medical care". For that to happen, one more thing needs to be addressed, and it's arguably more complex than any technical hurdle: the cost of treatment.

Gene editing is, or could be, a great leveller in healthcare. But like all experimental treatments, it is research-heavy, labour-intensive and expensive. One of Doudna's fears is that it will become a boutique technology, available only to those who can afford it. This, she says, would not only exacerbate the health gap that already exists between rich and poor, but also create a new kind of health inequality, a gene gap.

WHO DECIDES?

Given the enormous breadth of potential gene-editing applications, who gets to decide which ones are ethical and which ones are not? And if international standards differ, does it lead to a genetic arms race in which gene editing becomes a competitive imperative?



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The IGI is a non-profit, funded publicly and via philanthropy. Its staff talk of their work not just in technological terms but societal ones too, focused on how to maximise the reach of the technology.

"It's a major problem," Urnov says. "In the US, [some of] these medicines are sold for $2m, but European countries have refused to even licence them. You have a surreal situation where parents in Europe, whose children have these severe diseases, start GoFundMe campaigns to be able to pay American prices. We have this gap between the fact that this technology is rapidly expanding in its utility and we are struggling, frankly, with how to make it equitable and affordable."

Add to that the issue of health justice, the fact that if you're born with an inherited condition, an affordable cure may be possible if enough people have the same illness. That would make it economically viable for pharmaceutical companies to invest in the research to develop new treatments.

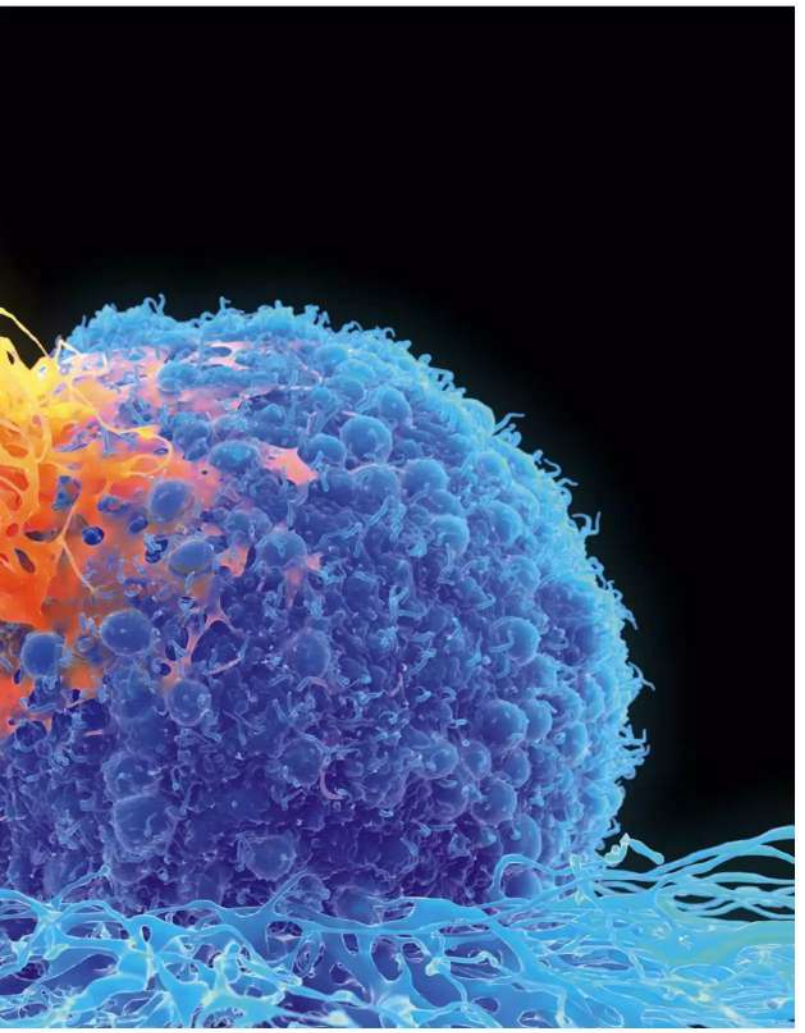
If you're born with a rare genetic mutation, that may not be possible. "There is this horrific gap between our ability to read that person's DNA and say, 'Yes, this is the mutation that killed your mom and will kill you, I'm sorry to say', and actually developing a treatment that would help that person. Developing such personalised cures has essentially no commercial value. Nobody will ever make money," says Urnov.

Lovell-Badge agrees. "The cost is a problem for it becoming really useful for public health," he says. "[We need to] start off from the very beginning thinking, 'How can we do this in a way that's going to be more affordable?' Then you approach the problem in a different way."

Unlike so much of the biotech industry, addressing this issue is a cornerstone that the IGI was built on – not just developing novel treatments, but creating scalable pipelines for discovery, testing and rollout.

"Our mission really has to be ensuring that technology benefits everyone," Doudna says. "That was the impetus for the Innovative Genomics Institute in the first place. Many institutes, many companies, many academic labs are now developing gene editing, but not with an eye towards controlling cost and doing the science with a focus on public access to that technology. That's really our purpose."

The genetic revolution is coming. After pioneering the technology, Doudna is adamant that when it arrives, it's available to everybody. As more than one of her colleagues tells us, that's just in her DNA. **SF**



ABOVE LEFT Chinese scientist He Jiankui hit the headlines in 2018 for using CRISPR to create the first genetically edited human babies. The press coverage soon turned sour when it emerged that the experiments had been carried out in an unethical manner. Jiankui is now serving a three-year prison sentence

LEFT T-cells (orange) are an important part of the immune system. Scientists could use CRISPR to modify the cells so they could potentially lead to treatments for cancer (blue), cardiovascular disease and arthritis

by IAN TAYLOR
(@IanStean)
Ian is former deputy editor of BBC Science Focus *and a science writer who focuses on health and future technology.*

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COMMENT

DOES CANNABIS LIVE UP TO THE HYPE?

Do the CBD-containing products on supermarket shelves really offer any health benefits?

Cannabis has been around for an awfully long time. There is evidence that it was being used in China as a medicine as long ago as 2600 BC, and I'm fairly sure that at least some Chinese people would have been using it recreationally.

But what has happened over the last few years is unprecedented, with an enormous surge in interest in cannabis-related products, to the point where it is being added to everything from dog food to chocolate to shampoo. The problem with all this hype is there is remarkably little evidence about genuine effectiveness.

It is certainly an interesting plant, containing more than 500 different compounds, many of which interact with 'cannabinoid' receptors in our bodies. One reason why cannabis has such wide and varying effects is because our bodies are riddled with these receptors, which help regulate sleep, stress, pain, appetite, memory and mood.

This in turn helps explain why people are now using cannabis products to treat a whole range of different conditions, but the two that stand out are chronic pain and severe childhood epilepsy.

In 2018, medical cannabis made the headlines in the UK thanks to Billy Caldwell, a young boy who suffered up to 300 epileptic seizures a day. Unable to get cannabis on the NHS, his mother travelled to Canada and was later stopped at Heathrow Airport and had the cannabis oil she was carrying removed.

"It is rare for patients to be prescribed cannabis oil for medical use on the NHS"

Since then, the National Institute for Health and Care Excellence (NICE) has taken a look at the research and on its website lists the conditions where it believes medically prescribed cannabis products might be helpful.

These conditions are chemotherapy-induced nausea and vomiting, chronic pain (as part of a clinical trial), moderate to severe muscle spasms caused by multiple sclerosis, and severe childhood epilepsy that has not responded to other treatments.

Despite this, and even though it is legal in the UK for specialist doctors to prescribe cannabis oil for medicinal use, it is rare for patients to get such treatments on the NHS.

Using cannabis in something like shampoo is far less contentious, but also less likely to be effective. The reason you might want to add it to something like shampoo is because one the main active ingredients in cannabis, cannabidiol (CBD), has been shown to act on cannabinoid receptors in the body to help reduce inflammation. This means it has the potential, if you rub it on your scalp, to improve things like dandruff, eczema and an itchy, flaky scalp. Whether it does is another matter.

When I checked out the website of a leading brand they were careful to point out that there is no evidence that a CBD-based shampoo will help your hair regrow or that "CBD shampoo can treat, prevent or cure any hair or skin conditions you may have". Though they do add that it may help dandruff and "can maintain moisture levels within the hair".

I think I will stick to my ordinary brand. **SF**

MICHAEL MOSLEY

Michael is a writer and broadcaster, who presents *Trust Me, I'm A Doctor*. His latest book is *COVID-19: Everything You Need To Know About Coronavirus And The Race For The Vaccine* (£6.99, Short Books).

BBC TWO

PORTRAIT: KATE COPELAND ILLUSTRATION: JASON RAISH

COMMENT

WHY WE STILL NEED COLD, HARD CASH

The modern, cashless way of paying with a simple tap of our phones has edged out some of the most vulnerable members of society

ALEKS KROTOSKI

Aleks is a social psychologist, broadcaster and journalist. She presents *The Digital Human*.

BBC RADIO 4 92–95 FM & 198 LW

Any change helps," said the man on the subway, looking around for some charity. Most of us buried our heads into our phones further, pretending that economic disparity was somebody else's problem. I thought about what was in my bag. My phone, a water bottle, an orange and an empty wallet. Because who carries cash these days? My next thought: I wonder if he takes PayPal?

I got out of the habit of carrying cash when we lived in Los Angeles. Many shops were moving away from using paper money, and it felt totally futuristic to pay for lunch with the tap of my phone. Some of the big chains had already gone completely cashless. As the owner of both a phone and a bank account to link it to, 'tap and go' quickly became normal for me and many others. Cash felt somehow subordinate, and weirdly seedy.

The pandemic accelerated a lot of things that have long been predicted by digital advocates: remote working, video conferencing, and making memories in *Minecraft*. It also accelerated the number of digital transactions that we do. In March 2020, only 10 per cent of transactions in small businesses were cashless, according to a report from digital payments company Square. That figure jumped to 60 per cent in June 2020. And for restaurants and other service organisations that were already processing 90 per cent of bills on a credit card, tripping into cashless was easy. Sweden, where only 1.3 per cent of GDP is circulated in cash, announced it was going totally cashless by 2023: no more hard currency transactions! Soon, we would all be liberated from those pesky pieces of metal and paper that have weighed down our pockets for millennia.

"'Tap and go' quickly became normal. Cash felt subordinate, and weirdly seedy"

The problem is, not everyone has access to a bank account and a mobile phone. One in five Americans were unbanked or under banked in the US in 2020, according to an economic wellbeing report from the Federal Reserve Board. They are predominantly the poor and the elderly, and disproportionately people of colour. They may be people who experience domestic abuse, or who are facing homelessness. The move to cashlessness has excluded them further, and created even more systemic barriers to overcome in order to participate fully in society. According to a survey from Which?, 1 in 10 people in the UK were refused service in shops for trying to pay with physical currency between March and July last year. So what happens when you have no alternative?

We have spent the last year facing the edges of the digital optimist's dream, and now we are correcting course. Sweden has since made conditions for cash to continue, and cities across the US have banned stores from refusing to take legal tender. Meanwhile, in the UK, contactless donation points have been installed on walls in cities that you can 'tap-to-donate'. The proceeds – more than £250,000 so far – have been distributed to homeless charities.

We need to urgently find more solutions to this divide. Eviction moratoria are expiring, government cheques are drying up and high streets have gone bust. Poverty isn't going away; and it certainly doesn't take PayPal. **SF**

PORTRAIT: KATE COPELAND. ILLUSTRATION: SCOTT BALMER

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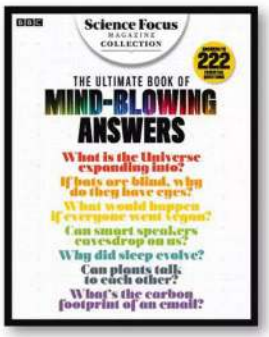
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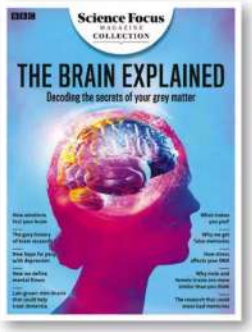

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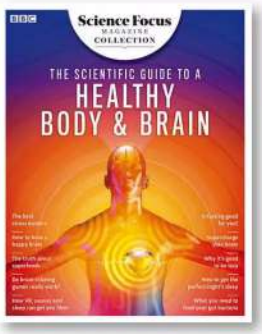

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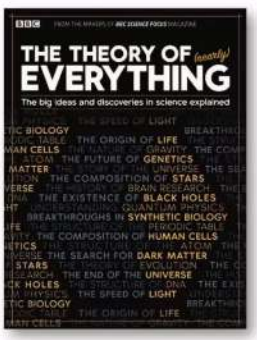

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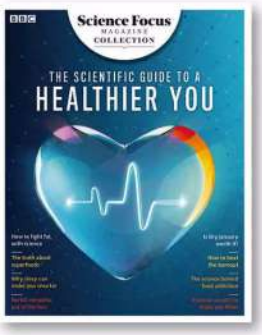

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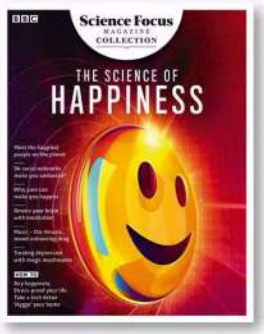

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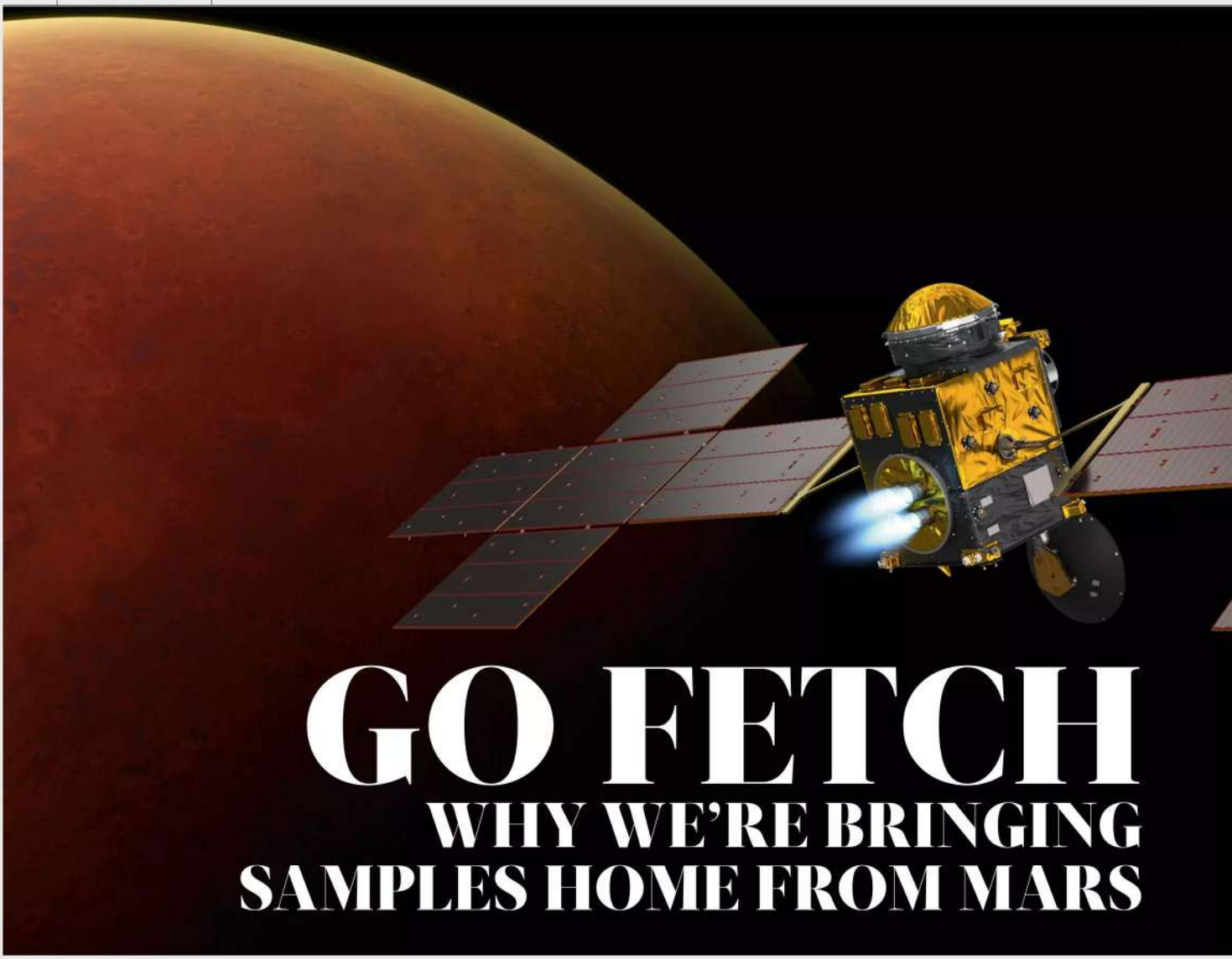

GO FETCH

WHY WE'RE BRINGING SAMPLES HOME FROM MARS

TELL US ABOUT THE SAMPLE RETURN MISSION.

The Mars Sample Return mission is the first mission – programme actually, because more than one craft is required – to return samples from another planet. We have samples from the Moon returned by the Apollo missions, by the Russian rover and most recently by the Chinese. And we've returned samples from asteroids [via missions run] by the US and Japan. But we've yet to return a sample from Mars. That's the objective. The first step is the Perseverance rover, which is beginning to collect samples after NASA landed it successfully on Mars in February this year.

The Mars Sample Return programme is a joint endeavour between NASA and the European Space Agency (ESA), although NASA is leading it. NASA will be responsible for the rockets that will launch from the surface of Mars and put the samples in Mars orbit. But ESA is responsible for the Earth Return Orbiter, which is basically going to be the first interplanetary spacecraft. It'll go from Earth to Mars, go into orbit around Mars, rendezvous with the sample craft in Mars orbit, capture the sample and then come back to Earth. It won't enter Earth orbit, but it'll release the NASA-built entry capsule containing the samples once it's near enough. Only the entry capsule will come back to Earth, not the Earth Return Orbiter. The plan is to essentially have the capsule perform a controlled crash. So we'll target the crash site, then have the Earth Return Orbiter release the samples and fly away. It'll deviate so that it flies past Earth and goes into a graveyard orbit around the Sun.

But prior to all this, Perseverance will be on Mars collecting samples. Those samples will be put in caches on the surface. In 2026 NASA will launch another rocket to Mars containing a lander that's carrying the Mars Ascent Vehicle and the Sample Fetch Rover. The lander will land on Mars and release the Fetch Rover, which will pick up the

DR ALBERT HALDEMANN
Albert is the ExoMars Payload and Assembly, Integration and Verification Team Leader at ESA, and he coordinates with NASA to keep the two agencies working smoothly together.

We want to bring something back from Mars. That's the thinking behind a programme so ambitious that it will take two space agencies and several missions to pull it off. To find out what's at stake, and how we'll get a sample from the Red Planet, **Sara Rigby** spoke to ESA's payload manager **Dr Albert Haldemann**

ESA

caches of rock samples that have been collected by Perseverance. The Fetch Rover will then bring them back to the lander, where they'll be put in the Mars Ascent Vehicle and launched into Mars orbit.

LAUNCHING ROCKETS FROM EARTH IS TRICKY ENOUGH. LAUNCHING ONE FROM MARS SOUNDS INCREDIBLY DIFFICULT.

Yes, there are plenty of challenges, especially as the launch will have to be carried out automatically.

The rocket will be a two-stage, solid-fuelled rocket, and that will carry the Orbiting Sample container – or OS, essentially a football-sized sphere. When the rocket gets into orbit, it'll eject the OS and leave it orbiting Mars.

We're still working on how best to make sure we can find it. Our baseline is that we make it shiny and use cameras to spot it from a distance of a few thousand kilometres, which is what the Earth Return Orbiter will be at as it makes its approach. It seems doable, but everybody's still a little worried. So we're considering about radio beacons, laser range finders and stuff like that. But there are a lot of challenging steps, which is what makes this fun for engineers who have to build all of these things and make them work.

WHAT WOULD IT MEAN TO THE ASTRONOMICAL COMMUNITY TO GET A SAMPLE OF MARS BACK TO EARTH?

We've sampled Mars from afar with our robots, rovers and landers. And we have samples from meteorites that were blown off Mars and landed on Earth. We know that's where they came from, thanks to isotopic analysis of the rocks. A few of them contain gas bubbles that are dead ringers for Mars's atmosphere, which we measured with Viking 1 and 2 back in 1976 and 1977.

WHY BRING BACK MORE SAMPLES FROM MARS?

Well, firstly we can't tell precisely where these Martian meteorites came from on Mars. We have some hypotheses, but we don't know. Secondly, although ➲

THE MARS SAMPLE RELAY The steps to bring Martian rock back to Earth

1. LAND, EXPLORE, DRILL
Launched in July 2020, NASA's Perseverance rover successfully landed in the Jezero Crater on Mars in February 2021. The roughly hatchback-sized rover represents the first leg of humanity's first round trip to another planet. The rover will use its drill to collect rock and soil samples and store them on the planet's surface.

2. SEAL AND DEPOSIT
Any samples Perseverance collects will be in sealed tubes that the rover will deposit on the planet's surface, essentially leaving a trail of breadcrumbs behind it as it explores the Martian surface. Future missions to Mars – collaborative efforts by NASA and ESA – will follow the trail left by Perseverance, to retrieve the samples and return them to Earth.

3. SET OFF THE SECOND WAVE
The next stage will get underway in 2026, when NASA launches another mission to Mars that will carry a lander containing the rover, rocket and capsule needed to collect the samples gathered by Perseverance and launch them on their journey back to Earth. The lander will aim to set down in the Jezero Crater, where Perseverance began its journey.

4. UNFOLD AND UNLOAD
After the lander has successfully touched down on the Red Planet, it'll deploy its solar panels to power up the ESA-designed Fetch Rover. The rover (a four-wheeled vehicle, slightly smaller than Perseverance) will then unfold itself and deploy from the lander before beginning to follow the trail of samples left behind by Perseverance.

we have high-powered instruments and spectrometers on Perseverance, and other Mars rovers, those instruments are miniaturised so they can make the trip; they're not as high-performance as the instruments we have in our labs on Earth.

Also, some of the rocks that will be obtained by Perseverance in the Jezero Crater aren't represented in the meteorite samples. Those kind of rocks don't survive being blown off of a planet, we think. And yet they're key to the geologic history of Mars. And because of the delta in Jezero Crater, the rocks from there might have been associated with liquid water and so are most likely to contain evidence of past life or organic materials of a past environment on Mars. Whether we decide that means there was or wasn't once life on Mars, we don't know yet. Let's wait for the evidence.

WHAT SORT OF THINGS WILL YOU BE LOOKING FOR IN THE SAMPLES?

That's down the road. But in order to analyse them, we're going to take extraordinary precautions. Because Mars is considered potentially inhabitable – we've seen that there are underground environments that may contain liquid water – for these first samples we'll use the most stringent planetary protection measures. The samples will be contained within rugged metal test tubes that are as inert as possible so we don't contaminate the contents. They'll be packaged inside the OS, which has multiple shells. Then, when the OS gets up to the Earth Return Orbiter, it's packaged inside the entry capsule that will also have multiple shells. And when the capsule gets back to Earth, it'll be picked up and bagged before being taken to a special facility for unpacking.

We'll X-ray the test tubes to see the mineralogy of the contents before we open them. Some of the samples may also undergo very high-energy synchrotron examination to look at their compositions.

Only once we're convinced that it's safe to do so will we open the capsules, and we'll do that in a controlled way too. Then other, more advanced geochemical procedures will be applied to the samples to look at the details and see if there are any organic materials along with the mineral.

THE SAMPLE FETCH ROVER LOOKS LIKE IT'S GOING TO HAVE INFLATABLE TYRES ON ITS WHEELS. WHY?

Yeah, they do look like inflated tyres. They're

5. GRAB AND GO
The Fetch Rover will follow in Perseverance's tracks to collect the samples that have been deposited on the surface. Once a sample has been located, a robotic arm will deploy to collect it and store it inside the rover, before it moves on to find the next one. Once enough samples have been collected, the Fetch Rover will return to the lander.

6. HAND OVER THE SAMPLES
Once the Fetch Rover has arrived back at the lander, the same arm it used to collect the sealed samples will transfer them into the nose cone of the Mars Ascent Vehicle, stowed inside the lander. If there are additional samples that the Fetch Rover was unable to collect, they could be brought to the lander directly by Perseverance.

7. BLAST OFF FOR HOME
Once the samples are loaded onto the Mars Ascent Vehicle, the small rocket will be launched from the lander into Mars orbit. The gravity on Mars is about a third of that on Earth, so it's easier for objects to reach escape velocity, hence the rocket can be much smaller. It's expected to be a maximum of 3m tall and around 50cm in diameter.

8. PICK UP AND DROP OFF
The Mars Ascent Vehicle will carry the container of samples into orbit around Mars and release it. Another spacecraft, the Earth Return Orbiter, will detect the sample container and collect it, before returning to Earth. Once there, the Earth Return Orbiter will drop the sample container into Earth's atmosphere... if everything goes according to plan.

NASA/JPL-X8

"PERSONALLY, I'M NOT WORRIED ABOUT MARS CONTAMINATION. I THINK EARTH AND MARS HAVE BEEN 'SHARING SPIT' FOR BILLIONS OF YEARS"

not, though – they're actually a wire mesh made with memory metal that allows us to make a bigger wheel that can be compressed in a smaller package for launch. The tyres do expand, but they don't inflate through air. When we get to Mars, they're released and allowed to expand to their full size. The reason for that is the Sample Fetch Rover will need to cover a lot of ground quickly, and larger wheels will help it do that.

We're also going to use just four wheels instead of the six we've had in previous designs. Six wheels is very efficient for rough terrain. Four wheels with big tyres, like you see on dune buggies, are also okay for rough terrain, especially if you know what the terrain is like, which we will, to some extent, because we have Perseverance on the ground already essentially doing reconnaissance.

ARE YOU WORRIED ABOUT CONTAMINATION FROM THE MARS SAMPLES?

Personally, I'm not worried about Mars contamination. I think Earth and Mars have been 'sharing spit' for billions of years. But my opinion is irrelevant compared to what the public and political perception is of this risk. So we need to address that. It's going to be a heck of a challenge, I think, especially given what we've seen with COVID as far as the general public's confidence in scientific authority is concerned. We've already taken our lesson from that.

And we welcome the challenge because we need to understand what the samples from Mars mean, if we ever want to have astronauts go there and come back. We need a detailed understanding of what planetary protection means if we have the ambition, as many do, to have astronauts – human beings – go further into the Solar System and then be able to come back to Earth. **SF**

BRAINDEAD BUT NOT FORGOTTEN

What can preserved human brains tell us about the past?

by **Hayley Bennett**

When we die, nature wastes no time in disposing of us. Within minutes, our enzymes get to work on our tissues, breaking down proteins and fats. Not long after, microbes that once inhabited our gut move through our body via our blood and begin the process of putrefaction that liquefies our organs. Our soft tissues usually disappear completely within five years to a decade, leaving nothing but bones and empty spaces – exactly what archaeologists expect to find when they're dealing with human remains.

That's why, when an archaeologist turns over a skull, the last thing they imagine being confronted with is a brain. But it does happen. When the conditions are exactly right, when death occurs in a particular way, the brain can survive for hundreds and sometimes thousands of years. It may be shrivelled, waxy, brittle or glassy. But key structures like the brain stem, the characteristic grooves and folds of brain tissue, and even ancient proteins can be preserved in centuries-old organs.

Some experts now think that brains are being preserved more often we realise; it's just that archaeologists don't always have the experience to recognise them. "Now that there's more literature about it, more of these brains will come to light and we'll be able to put them at different points on the time scale of millennia and analyse them," says neurologist Dr Axel Petzold, who worked on the decapitated Yorkshire man's brain (see p73).

What, though, can preserved brains reveal about the bodies they once inhabited? Could they help us to uncover secrets about the past, solve mysterious deaths or catch ugly crimes? And, perhaps most intriguingly, how did these squidgy masses of fatty tissue manage to survive the ravages of time at all? ➤

ALAMY

1. FROZEN IN TIME

AGE: 5,300 YEARS
LOCATION: TYROLEAN ALPS, AUSTRIA
DISCOVERED: 1991

Considered something of a record-holder in the preservation stakes, the Tyrolean Iceman dubbed 'Ötzi' endured 5,300 years on a ridge high in the Tyrolean Alps before being discovered by a pair of German tourists in the early 1990s. He was so solidly frozen into the ice that he had to be dug out with a pneumatic drill, ski poles and ice picks. Though half-decomposed, he was doing well for his age, so much so that scientists were able to piece together everything from what he ate for his last meal (ibex), to what his underwear was made of (leather), as well as his genome.

Ötzi did keep something to himself though: his brain has never been examined by human hands or eyes. We do however, have scans and samples from it. Scientists led by Dr William Murphy at the University of Texas imaged the skull by X-ray and CT scan, revealing a brain that was shrunken, but preserved by what's known as adipocere or 'corpse wax'. This solid, waxy substance develops in the months after death through chemical reactions involving fats and water.

Compared to soft tissues elsewhere in his body, Ötzi's brain was better preserved, supposedly due to higher levels of water that helped form the corpse wax. "The fact that brain tissue is relatively protected from the ambient environment by the skull provides an opportunity for a higher-humidity environment for the brain than that for the rest of the body," the scientists wrote. "This difference could lead to relatively greater adipocere formation in the brain."

Separately, a European team of scientists took two tiny tissue biopsies from the Iceman's brain, studying them under the microscope to reveal neuron-like structures and red blood cells, and extracting over 500 preserved proteins, some of which they could match to his genome sequence. They found numerous proteins related to stress responses and bleeding. "These proteins could support the theory of an injury of the head near the site where the samples have been extracted," they wrote, delivering a potentially fatal blow to the previously favoured theory of Ötzi's death: a fatal arrow wound.

Ötzi the Tyrolean Iceman's body had spent over 5,000 years buried in ice. Scans of his brain suggest it's endured better than the soft tissue of his limbs

2. PROTEIN-PACKED

AGE: 2,600 YEARS
LOCATION: YORKSHIRE, UK
DISCOVERED: 2008

Sometimes unremarkable sites conceal remarkable discoveries. Such was the case in 2008, when archaeologists working at a dig on a University of York campus uncovered an Iron Age farming landscape littered with pottery and flint. The most surprising find was in a wet pit marked by a single stake: a decapitated human skull. It wasn't until the skull was being cleaned back at York Archaeological Trust's headquarters that something was found rattling around inside it.

Although shrunken, scans confirmed that the beheaded man's skull contained a brain. This was puzzling, since the conditions didn't offer anything to suggest what would have preserved it and there was no hair or other soft tissue. When the skull was eventually opened, the brain tissue turned out to be very acidic. Dr Axel Petzold, a neurologist at University College London, was present at the time and remembers seeing a knife "turned black with erosion" as it cut into the brain.

One theory is that the victim's head was dropped into acid. This could explain why the 800 or so proteins that Petzold later extracted from the tissue were so well-preserved. "In the laboratory, if I want to preserve proteins, I can just put them in acid," explains Petzold. This theory also tallies with results published last year showing that more of the proteins in the outer parts of the brain survived, compared to the inner parts, suggesting that some unknown substance diffused in.

There's more to the mystery though. When Petzold's team was trying to extract the proteins, a lot of them seemed to be stuck inside an insoluble brown muck. Then, in their long-term decay experiments on the brain tissue, protein levels started going up rather than down as they would have expected. It seemed the proteins had aggregated and were now being released. Petzold explains the long nerve fibres in the brain contain very flexible proteins that can change their shape. "We think that's how the brain got preserved," he says. "Over time they just folded in or aggregated."

Ordinarily, proteins don't aggregate like this, but mutations in one protein suggested that the decapitated man was in the grip of a rare neurological condition known as Alexander Disease, which causes seizures and problems with movement and speech. The disease is also linked to protein aggregation. It's a little speculative, but Petzold says these results provide a plausible explanation as to why the man was killed: his symptoms, which were not understood at that time, may have marked him out as a mad man.

1. The decapitated skull recovered from the University of York. The dark brown surface indicates oxidation

2. The brain covered with muddy sediment

3. The surface markings on the fractured second vertebra suggest that decapitation may have been the cause of death

4. Careful cleaning of the brain surface by researcher Sonia O'Connor

5. The cleaned brain revealing the preserved, albeit shrunken structures termed 'gyri and sulci'

EURAC RESEARCH, AXEL PETZOLD X5

Could the extreme temperatures in the aftermath of the Vesuvius eruption have turned the brains of those caught in the blast into glass?

3. HOT DEBATE

AGE: 1,492 YEARS (79 AD)
LOCATION: CAMPANIA, ITALY
DISCOVERED: 1960s (BRAINS REPORTED 2020)

In the first century AD, a cataclysmic eruption of Mount Vesuvius devastated the Roman town of Herculaneum. Archaeologists discovered 330 bodies here, and more at Pompeii and other Roman settlements, mainly those of people who died when their homes collapsed on them. One victim – left like a macabre museum exhibit – remains forever sheltering in his bed, his skull scattered about like pieces of broken pottery. His head, it seems, exploded in the heat of the volcanic eruption and resulting ash cloud.

The victim's skeleton was discovered in the 1960s, but is still giving up its secrets. "Almost 60 years later, during a site investigation, I saw something shining within the volcanic ash filling the skull," says Pier Paolo Petrone, a researcher at the University of Naples Federico II. "A glassy black material." The black stuff was stuck to the insides of the skull fragments, leading Petrone to the natural conclusion, in a 2020 study, that whatever had produced it had come from inside the victim's head.

Petrone's team set out to prove that it was in fact 'vitrified' brain tissue that had been turned to glass in the heat of the volcanic eruption and then buried. As Petrone explains, "I proposed that the brain was preserved due to the rapid drop of the initially very high temperature of the first pyroclastic surge." Vitrification, which turns a liquid to a solid, but without forming crystals, is also used to cryopreserve frozen eggs, sperm and embryos in fertility treatments.

The study incited some nit-picking among archaeologists over vitrification temperatures, as well as about preserved ancient proteins that Petrone's team claimed to have identified in the glass – none of them matched the proteins found in Ötzi's or the beheaded Yorkshire man's brain. Petrone says the preservation of the structures in the ancient brain is exceptional however, and will allow it to be studied "at a level of resolution never seen before."

PIER PAOLO PETRONE/UNIVERSITY FEDERICO II OF NAPLES/ITALY, JOHAN REINHARD X2

4. MOUNTAIN MUMMIES

AGE: 500 YEARS
LOCATION: LLULLAILLACO MOUNTAIN, ARGENTINA
DISCOVERED: 1999

High in the Andes, a combination of below freezing temperatures, low oxygen levels and humidity naturally mummifies those who die in the mountains. These conditions contributed to the extraordinary preservation of three frozen children sacrificed by the Incas. After they were recovered in 1999, scientists wrapped them in plastic inside individual freezers to maintain their humidity and keep them from disintegrating.

The children (two girls and a boy) apparently froze soon after death, halting decay before it could take hold. In 2016, explorer Johan Reinhard described his surprise when pulling back a blanket covering the youngest girl's head. "None of us had expected to see her face, much less that it would exhibit a pensive stare," he wrote.

Almost all of the children's organs appeared in scans, with blood still present in hearts and lungs, making them some of the best-preserved mummies ever found. However, their brains have never been directly sampled.

In 2003, a team including Reinhard published CT scans of the children's brains. The spaces between their skulls and brains showed the brains had shrunk (as with the Iceman, although perhaps to a lesser extent) but the researchers were able to tell the grey and white matter apart. "The fatty tissue of the bodies and the white matter... were visibly white on the CT scans," they wrote. They suggest the white matter appeared like this due to reactions in corpse wax that combine fatty acids and minerals to produce soap.

As for the cause of death, head trauma was ruled out by the CT scans, leading scientists to propose they were buried alive or suffocated. More recently, analysis of the oldest child's hair suggests she was plied with drugs and alcohol to keep her sedated. According to a 2015 study, the Incas rarely carried out bloody rituals as bloodshed would have made the sacrifices 'incomplete'.

FAR LEFT Care had to be taken to maintain the conditions in which the mummified children were found

LEFT CT scans showed the children's brains had shrunk in their skulls

BELOW The cold and high-altitude conditions preserved the children's bodies remarkably well

5. HARDBOILED

Age: 4,000 years
Location: Kütahya, western Turkey
Discovered: 2010

There's something 'special' about the earth at Seyitömer Höyük in Turkey, insists biologist Meric Altinoz. In his view, it's no coincidence that the same soil that preserved the brains of four Bronze Age fire victims also preserved lentil seeds that he was still able to germinate 4,000 years later. "[It's] a unique environment, which somehow preserved both the brains and the seeds," Altinoz says.

Seyitömer Höyük is an ancient burial mound thought to have been formed over the site of an earthquake and fire. Four of the partially burned skeletons uncovered there were found with their brains poking out of their cracked skulls. Though he now works with neurosurgeons, Altinoz was part of a Turkish team that, in 2014, analysed the preserved brains along with the soil they were buried in – clay that supplied the nearby city of Kütahya's ceramic industry.

Altinoz refers to the shrunken and hardened Seyitömer brains as "bioporcellate" – not dissimilar in texture, he notes, to the ceramics that were produced in the local area. Their fat content showed clear evidence of corpse wax, but when the researchers looked in detail at their mineral composition, they found that they contained high levels of alkaline minerals, such as potassium and magnesium, which are present in clays, as well as boron, used in tile-glazing, but also mummification. "It was even higher than the boron level that was used for the mummification of Egyptian brains," says Altinoz.

While water is usually thought to be important for forming corpse wax or adipocere, here, there was only fire. The team therefore theorise that the brains boiled in their own tissue water after death. Similar high-temperature reactions are used in industry to produce stearic acid – the main fatty acid component of adipocere – from animal fats. The clay minerals in the soil would also have helped make the wax harder and more brittle.

What about the boron, though? Although it's just speculation, Altinoz remains convinced it played a role in keeping the brains and the seeds preserved – boron is known to help stop plants from rotting, he points out. Unfortunately, he was never able to glean much from the lentils, because his fridge broke, killing the last remaining

ABOVE
The preserved brains as they were found

RIGHT
The brains were shrunken and hardened by the conditions, taking on an almost ceramic look and feel

BELOW
The ruins of the early Bronze Age settlement at Seyitömer Höyük, where the preserved brains were discovered

MERIC ALTINOZ X5, ALAMY

Dr Fernando Serrulla examines one of the 45 brains preserved in and recovered from the La Pedraja mass grave

6. LOST AND FOUND

Age: 85 years
Location: Villafranca de Montes de Oca, northern Spain
Discovered: 2010

Even when burial sites are relatively modern, archaeologists don't expect to find brains in them, much less 45 of the organs. Yet a team working at the excavation of La Pedraja mass grave, near the city of Burgos in northern Spain, uncovered the largest and best preserved collection of brains in the world.

The 45 brains belong to the victims of fascist rebels supporting General Franco's 1936 military coup, just a few of the approximately 130,000 Spanish people executed at the time. Many more would die in the Spanish Civil War that followed. Sadly, most were never returned to their families and remain in mass graves. At La Pedraja, 104 bodies were exhumed from the 1.5m-deep pit by the Aranzadi Society of Sciences, aided by volunteers. The grave was still new enough to be classed as a crime scene and was scrutinised by forensic experts as well as archaeologists.

"When we dug the pit it still smelled of decomposition 80 years later," says Dr Fernando Serulla, one of the forensic experts from the Hospital de Verin who attended the site in August 2010. Serulla personally found at least five of the 45 preserved brains, which had shrunken to less than a third of their original size and were greasy to the touch.

Serulla went on to lead a 2016 study on the brains. The main reason they remained in such good condition, while the bones deteriorated badly, he says, was the presence of a lot of water. "The perpetrators dug in soft, moist earth and left the bodies between July and September 1936, months that were unusually rainy." As in other cases, it's thought the water contributed to the chemical reactions that turn fatty tissues to corpse wax, protecting the brains. Serulla also thinks that blood emptying from gunshot wounds to the head prevented the putrefaction by bacteria that would normally start soon after death.

Besides being an interesting case of exceptional preservation, Serulla says studying these brains opens the door to investigation of serious crimes such as torture. "We've managed in one of the cases to show that the person suffered brain injuries several days before he died," he says.

Only 18 people killed at La Pedraja have been identified, but all the victims have now been reburied together at a cemetery, beneath a memorial. **SF**

by HAYLEY BENNETT
Hayley is a freelance science writer and editor, based in Bristol.

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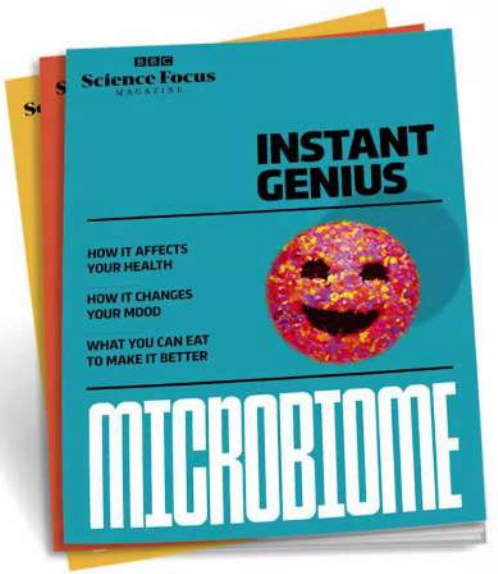

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Q&A

YOUR QUESTIONS ANSWERED

... ARE GIRAFFES MORE AT RISK FROM LIGHTNING?
... WHEN DID DINOSAURS BECOME BIRDS?
... WHY DON'T MICROPLASTICS KEEP BREAKING DOWN?
... IS TOO MUCH TESTOSTERONE MAKING ME A GRUMPY OLD MAN?
... BUT SERIOUSLY, WHAT COLOUR IS THE SUN?
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... IS PROCRASTINATION GENETIC?
... WHY HASN'T TIDAL POWER TAKEN OFF YET?

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DR ALASTAIR GUNN Astrophysics lecturer

DR ADAM HART Zoologist and science communicator

DR NISH MANEK Medical expert and GP trainee

DR HELEN PILCHER Biologist and science writer

LUIS VILLAZON Science and technology writer

ILLUSTRATION: DANIEL BRIGHT

VIKRAM RATHAUR, LONDON

HOW SIMILAR ARE TURTLE SHELLS TO HUMAN RIBS?

The upper shell of a turtle or tortoise is actually the ribcage. The individual ribs fuse together where they emerge from the spine and extend around the shoulders and pelvis of the animal to form a continuous carapace. The underside of the shell is a separate piece made from the shoulder girdle and sternum (breastbone). So turtles don't actually 'live inside' their shells, any more than you live inside your own rib cage. But the shell isn't made entirely of bone. It's covered with around 54 plates of horn-like keratin that provide waterproofing and scuff-protection. ***LV***

TOP TEN

HEAVIEST SPACECRAFT

Getting to space: it ain't easy – each kilogram needs an estimated 32,900,000 joules of energy just to reach low Earth orbit. Despite this hurdle, humans have launched vehicle after vehicle through the atmosphere and into space. But which is heaviest? These are the spacecraft with the largest mass to have flown in Earth's orbit and beyond.

1 **INTERNATIONAL SPACE STATION**
Space station, made of 16 pressurised modules
In service: 1998-present
419,725KG (2011 size)

2 **MIR**
Russian space station
In service: 1986-2001
140,000KG

3 **SPACE SHUTTLE**
US orbiter vehicle
In service: 1981-2011
110,000KG (Gross lift-off mass of *Endeavour*)

4 **BURAN**
Russian uncrewed spaceplane
In service: 1988
105,000KG (Orbiter vehicle mass)

5 **SKYLAB**
US space station
In service: 1973–1979
77,000KG

6 **APOLLO COMMAND AND SERVICE MODULE**
US lunar spacecraft
In service: 1968–1975
28,800KG

7 **TIANHE CORE MODULE**
Cornerstone of Chinese Tiangong space station
In service: April 2021-present
22,000KG

8 **SALYUT 7**
Russian space station
In service: 1982–1991
19,824KG

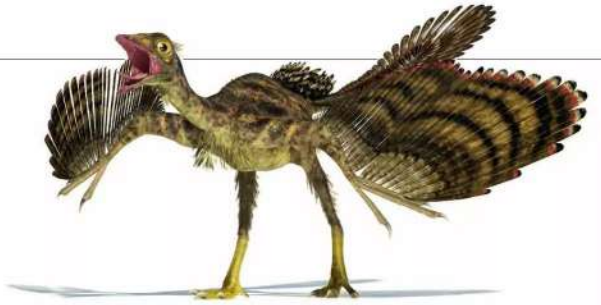
9 **ATV (AUTOMATED TRANSFER VEHICLE)**
European Space Agency cargo spacecraft
In service: 2008–2014
19,357KG

10 **SALYUT 1**
Russian space station
In service: 1971
18,900KG

KATHY WHITE, LIVERPOOL

ARE GIRAFFES MORE AT RISK FROM LIGHTNING?

Despite being around five metres tall, giraffes are very unlikely to get struck by lightning. But this is mainly because lightning and giraffes are both fairly rare. There are only five well-documented fatal strikes on giraffes between 1996 and 2010. With a global giraffe population of around 140,000 in that period, this is about 0.003 deaths per thousand giraffes per year. That's a very low risk, but it's still more than 30 times the equivalent fatality rate from lightning in humans in the US. ***LV***



EMILY BROWN, NOTTINGHAM

WHEN DID DINOSAURS BECOME BIRDS?

Today's birds evolved from dinosaurs, which makes them dinosaurs! The same way bats are mammals, birds are a strange type of dinosaur that got small, evolved wings and developed the ability to fly. Birds evolved from 'raptor' dinosaurs – the *Velociraptor* family. The oldest fossil of a true bird, defined as a dinosaur that could fly by flapping its wings, is *Archaeopteryx*, which lived about 150 million years ago in the Late Jurassic. But because close 'raptor' cousins of birds are known from earlier in the Jurassic, it's likely birds first took to the skies around 170 million years ago. ***SB***

CHARLOTTE LOWE, ST AUSTELL

WHY DON'T MICROPLASTICS KEEP BREAKING DOWN?

It's all about timescale. Microplastics do keep breaking down, but as the pieces get smaller, the decomposition rate slows. Most microplastics form when bigger bits of plastic break down in the environment, aided by sunlight, oxygen and friction. Microbes can also play a part in decomposition, depending on the type of plastic.

With all of these processes, the microplastics can continue to break down to form nanoplastics, which have diameters below one micrometre or one-thousandth of a millimetre. These are invisible to the naked eye and hard to detect using analytical kit, which is perhaps why we don't hear about them so much. ***ED***

NASA/JPL X3, NASA/ESA, ALAMY X3, SHUTTERSTOCK X2, GETTY IMAGES X4. ILLUSTRATIONS: DANIEL BRIGHT

DEAR DOCTOR...

HEALTH QUESTIONS DEALT WITH BY *SCIENCE FOCUS* EXPERTS

IS TOO MUCH TESTOSTERONE MAKING ME SUCH A GRUMPY OLD MAN?

Don't get angry, but it's the other way around – a low testosterone level is likely to cause irritability. While the term 'male menopause' is used for the condition, this phrase is a bit misleading – there isn't usually a sudden drop in testosterone in middle age like there is for oestrogen in women.

Testosterone levels do fall with age, but the decline is gradual – less than 2 per cent a year from about the age of 30 – and it doesn't usually cause any issues.

Rarely, testosterone can drop to a level that causes symptoms like tiredness, decreased sex drive, problems maintaining an erection, and irritability. But it's not that common. In 2010, the European Male Ageing Study (EMAS) found that testosterone deficiency affected about 2 per cent of men aged 40 to 79, and about 5 per cent of men aged 70 to 79.

True testosterone deficiency is rare, but is more likely in men who are overweight and/or have chronic conditions, such as type 2 diabetes. Specific genetic problems with the testes can also cause it, but these are exceptionally uncommon.

So, if you're feeling a bit grumpy, it's definitely not due to too much testosterone, but it is also unlikely to be a 'male menopause'. Lifestyle factors like poor sleep, alcohol and smoking, or mental health problems like stress, depression or anxiety, are more likely to be the culprit. ***NM***

DARREN RICHARDSON, WIMBLEDON

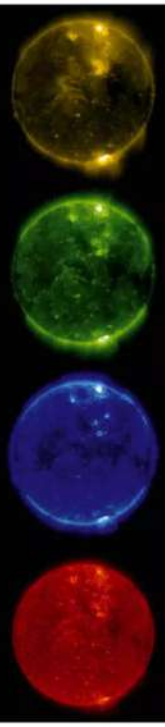
BUT SERIOUSLY, WHAT COLOUR IS THE SUN?

Not the yellow hue you'll find in your average school textbook.

The Sun emits light over a whole range of wavelengths (or colours). In fact, it does so in all parts of the electromagnetic spectrum, apart from gamma rays. The peak in the Sun's spectrum can be used to derive its surface temperature, about 5,780 Kelvin (roughly 5,500°C). The same process can be used to establish the surface temperatures of the stars.

The peak wavelength in a spectrum also generally determines an object's apparent colour. So, for example, cooler stars appear red and hotter stars appear blue, with orange, yellow and white stars in between. For the Sun, the spectrum actually peaks at a wavelength that we would normally describe as green. However, across the narrow range of the visible spectrum the amount of light emitted at each wavelength is almost exactly the same. But more crucially, the human eye doesn't perceive light by averaging the various colours of the spectrum together. So, a very slight excess of green light doesn't look green to the human eye – it looks white. The Sun would have to emit only green light for our eyes to perceive it as green.

This means the actual colour of the Sun is white. So, why does it generally look yellow? This is because the Earth's atmosphere scatters blue light more efficiently than red light. This slight deficit in blue light means the eye perceives the colour of the Sun as yellow. The more atmosphere the Sun's light passes through, the more blue light is scattered. Hence, during sunrises and sunsets there is a much greater percentage of red light in the Sun's spectrum, giving often spectacular results. ***AGu***



NASA/SOHO, SHUTTERSTOCK, GETTY IMAGES

CROWDSCIENCE

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IS MY NEIGHBOUR'S NOISE HARMING MY HEALTH?

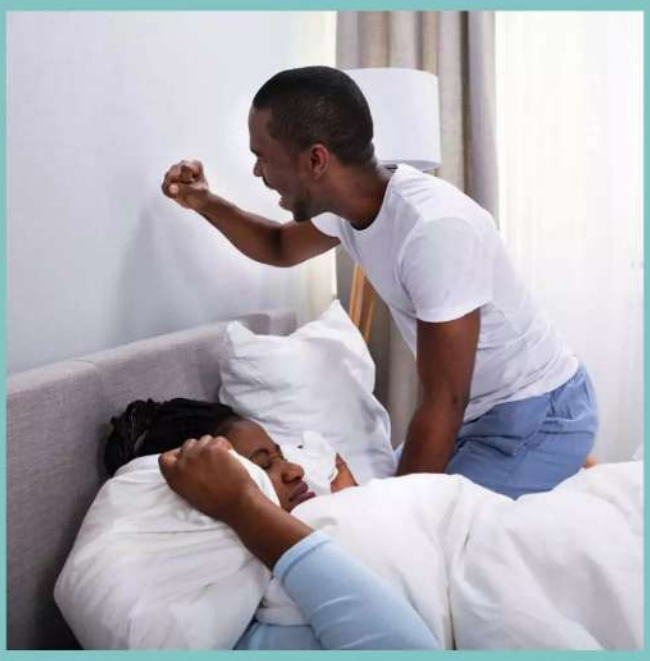
We've all felt annoyed by noises that are outside of our control, whether it be a car horn, construction work, or an inconsiderate neighbour's music. Regular exposure to sounds below 80 decibels (dB) won't physically harm our ears, but even quiet sounds can have long-term effects on our brains and bodies.

Road traffic and aircraft noise have been linked to impaired concentration, learning and memory, plus increased risk of cardiovascular disease. For example, one analysis found that for every 10dB increase in traffic noise, a person's risk of coronary heart disease rose by 8 per cent.

Less is known about how other types of noise impact health, but a 2019 study of nearly 4,000 Danish adults living in multistorey housing found that those who reported being annoyed by neighbours' noise were more likely to report problems like headaches, trouble sleeping, depression and anxiety.

Noise can disrupt our sleep – even if it's not loud enough to wake us – and poor-quality sleep can influence mood, concentration and lead to long-term harm by triggering our bodies' stress responses. However, researchers in the Netherlands even found neighbour noise was correlated with the incidence of joint pain, fatigue and cardiovascular disease, even when sleep loss was controlled for statistically.

Wildlife is also affected by the noisy human world. Some birds change the volume or frequency of their calls to cut through the city din and dolphins alter their behaviour and vocalisations to adapt to ship noise. ***CA***



Noble false widows can bite, but most people will only experience mild effects

LAURA ABERNETHY, BELFAST

ARE THERE ANY DANGEROUS SPIDERS IN THE UK?

There are around 650 species of spider in the UK, ranging from those with a leg span of just a couple of millimetres, to the 12cm leg span of the cardinal spider. Spiders are predators, and they use an impressive pair of fangs to catch prey and to introduce venom. All spiders have fangs, but not all spiders have fangs that are able to pierce human skin. Consequently, there are relatively few UK species that can bite us in any meaningful way.

The venom from most of the handful of UK species that can bite is less concerning than the puncture wound the bite causes. Fangs can introduce bacteria into the tiny wounds they create, so if you suspect you have been bitten by a spider it's best to clean the wound and use an antiseptic treatment. Just as with a wasp or bee sting, antihistamines may help with the swelling and itching, but if symptoms don't improve, get worse or develop into other symptoms then it's sensible to seek medical attention. Although it's rare, some people may be allergic to spider venom, with similar symptoms developing as with a bee or wasp sting allergy.

One spider that recent research suggests may be of some medical concern is the noble false widow spider *Steatoda nobilis*. This species was first recorded in the UK in Torquay in 1879, and has recently increased in abundance and range. The media have been quick to pick up on 'spider bite' stories, but it's often not possible to verify that the victim has been bitten by any spider, let alone a noble false widow.

Nonetheless, this species can bite and, because it seems to thrive in urban areas, and around our homes and outbuildings, we might expect to see more reports of bites as time goes on. However, for those few people that do, the vast majority will experience only very minor effects. ***AH***

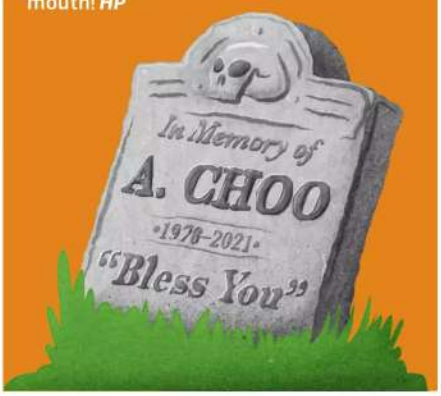
OLD WIVES' TALES...

DOES MY HEART STOP BEATING WHEN I SNEEZE?

Aaaaachooo! Sneezing, also known as sternutation, is the rapid and involuntary expulsion of air from the lungs through the nose and mouth. When you inhale before a sneeze, the pressure in your chest increases. Then, when you exhale during the act, the pressure drops. This causes a fleeting change to the heart rate, which quickly corrects itself. So, although you may *feel* like your heart has skipped a beat, the trusty muscle does not stop beating.

Sneezing can be good for you because it helps rid the body of respiratory irritants, such as pollen and dust. However, suppressing a sneeze, by holding your breath or pinching your nose, might even be bad for you. One computer simulation found that, compared with a normal sneeze, it can raise the pressure inside the airways by up to 24 times, resulting in possible damage. Injuries can range from relatively minor, like a ruptured eardrum or burst blood vessel in the nose, to the life-threatening, such as the rupturing of a brain aneurysm, or the trapping of air in the diaphragm leading to the collapse of the lungs.

Remember: sneeze, but sneeze with care. The activity can propel droplets and germs at speeds of up to 160km/h (100mph), so always cover your nose and mouth! ***HP***



ASTRONOMY FOR BEGINNERS

LOOKING SOUTH AT 1:20AM BST ON 20 AUGUST

HOW CAN I SEE JUPITER AT OPPOSITION?

WHEN: 19 AUGUST

August is quite often one of the quieter months in the astronomical calendar. With the Sun setting later through the summer months, it can make fainter objects challenging to observe.

The plus side is that warm weather makes it the perfect time for beginners to get to know the night sky without winter coats and woolly hats, however.

A particular gem is the king of the Solar System: Jupiter, which comes into opposition on 19 August.

As the outer planets orbit around the Sun, Earth occasionally finds itself between the Sun and another planet, with all three in direct alignment. When this happens, we describe it as a planet being in opposition.

Oppositions occur roughly annually (with Mars being the exception, at 27 months) and can often provide the best opportunity to observe and photograph the particular planet because of its favourable position and brightness.

At Jupiter's opposition, Earth will lie directly in between Jupiter and the Sun. It will appear bigger and brighter than usual as it's also when Earth and Jupiter's orbits are closest together (known as perigee).

From around 9:14pm, Jupiter will begin to rise in the eastern constellation of Capricorn, just 7° above the horizon. As the night progresses, it will climb until it reaches its highest point, 24° above the horizon at 12:20am (so you won't need to stay up too late to enjoy it). As dawn approaches, it will slowly descend, disappearing below the horizon at approximately 4:56am.

For naked-eye observers, Jupiter will appear as a very bright point of light that, unlike stars, does not twinkle. A decent set of binoculars (7x10 magnification) will provide you with a view of Jupiter's four largest moons, Ganymede, Europa, Callisto and Io, and a telescope will allow you to view Jupiter's stripes. ***NB***

HOW ARE LAB-GROWN DIAMONDS MADE?

Lab-grown diamonds have the same carbon structure as naturally occurring ones. But while the former is made over millions of years, the synthetic kind are formed in days or weeks.

They're generally grown using a high-pressure, high-temperature (HPHT) method. Scientists at General Electric designed the first HPHT method in 1954 to mimic diamond growth deep below the Earth's surface. HPHT is the most economical process for growing large diamonds. ***ED***

FELIX M, VIA EMAIL

IS PROCRASTINATION GENETIC?

Just can't bring yourself to start that work report? Blame your mum. Well, partly. As a seminal 2014 study of identical twins claimed, up to 46 per cent of your tendency to procrastinate can be explained by genetic factors. Although scientists haven't identified specific genes behind the problem, research has suggested those with a larger amygdala (a brain region associated with emotion processing), are more prone to poor self-control and delaying unpleasant tasks. If this sounds like you, don't beat yourself up: procrastinators who are able to forgive themselves for their bad habit are less likely to repeat it in future.

1 SOW THE SEED
The HPHT process begins with a tiny diamond fragment, known as a seed crystal. This is placed in a cell inside a press, together with a metal catalyst, such as nickel or iron. A block of pure carbon, such as graphite, sits on top.

2 APPLY PRESSURE
The press heats the cell to a searingly high temperature, up to 1,600°C. It then uses metal anvils to apply intense pressure. The pressure and temperature need to be high enough to melt the metal catalyst.

3 ATOMS ACCUMULATE
The molten metal carries carbon atoms from the graphite to the seed crystal. The carbon atoms slowly build up around the crystal to give the multi-sided structures that we know so well. The growth rate needs to be controlled to reduce the risk of faults.

4 CUT AND POLISH
After the diamond has been cooled, it's ready to be cut and polished, just like nature's finest. It can then be graded for cut, colour, carat and clarity. The catalysts can give the diamonds a touch of colour, depending on the type of metal.

QUESTION OF THE MONTH

JOHN AWBERY, READING

WHY HASN'T TIDAL POWER TAKEN OFF YET?

Although wave and tidal power have the potential to deliver 20 per cent of the UK's electricity needs, we receive less than 3 per cent of our energy in this way. While other renewable energy sources, such as wind or solar, have seen rapid growth in recent years, tidal power lags behind.

Tidal power uses underwater turbines to harness the phenomenal energy unleashed by rising and falling tides. Tidal farms typically use barrages or artificial lagoons to channel the flow of water, and newer types of turbines can be installed directly on the seafloor.

Unlike solar or wind power, which only generate electricity under the right weather conditions, tidal power can reliably be harnessed every day. The Moon's gravitational pull ensures two daily powerful tides across the globe.

Despite their low carbon credentials, tidal farms can spell trouble for the local environment. Turbines can injure marine animals and barrages restrict the movement of migratory species. The electromagnetic fields and noise generated are also a concern, particularly for animals that use echolocation.

However, the large price tag accompanying new tidal farms can make them a tricky proposition for politicians. Of five proposed projects in the Severn Estuary shortlisted by the UK government in 2008, the cheapest came in at £2.3bn, and none were greenlit.

Why is tidal so expensive? Some costs are unavoidable. Tidal farms need to be durable enough to withstand the force of the tides and their large size entails a vast quantity of construction materials, particularly concrete. But technology-related costs may fall: tidal power is still in its infancy and although expensive today, government support for tidal power may help costs tumble, following in the footsteps of offshore wind energy. ***AFC***

WINNER
John wins a **bundle of science non-fiction books from Bloomsbury**, worth £68. The prize includes *Beasts Before Us: The Untold Story Of Mammal Origins And Evolution*, by Elsa Panciroli; *Life Changing: How Humans Are Altering The Earth*, by Helen Pilcher; *Sway: Unravelling Unconscious Bias*, by Pragya Agarwal; and *Our Biggest Experiment: A History Of The Climate Crisis*, by Alice Bell.
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BEASTS BEFORE US

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GETTY IMAGES, ALAMY. ILLUSTRATIONS: DAN BRIGHT, PETE LAWRENCE

THE EXPLAINER

HOW CAN I BE A BETTER PARENT?

HOW CAN I MAKE BEDTIME EASIER?

There's a genetic component to our need for sleep, so the number of hours varies between families. However much sleep your child needs, they're far less likely to get it if they're checking their screens at bedtime. In a 2019 study of 6,000 adolescents, those who used their phones in bed were likely to get to sleep later and to have less refreshing sleep.

Most of us, adults and children alike, aren't getting enough sleep. But research shows that consistent bedtime behaviour work wonders. An online survey of over 1,000 families showed that a regular routine leads to better sleep for all the family. It doesn't matter what that routine consists of, as long as it's consistent. Sleep patterns are a matter of habit.

HOW IMPORTANT IS PLAYTIME?

Play is what teaches us how to be human. Children around the globe have been observed play-acting the things they see their parents doing. For example, in a study from 2011, Prof Artin Göncü and Prof Suzanne Gaskins watched four-year-olds at play around the world. Yucatán children play at making tortillas; children in urban Europe play at going to the office. Based on their observations, Göncü and Gaskins argue that play is a social apprenticeship – it allows children to understand and to prepare for their place in the world.

What's more, children learn better when they're allowed to be playful. For example, in 2009 Dr Karen McInnes and her colleagues at the University of South Wales gave children jigsaw puzzles to complete. Half of the group were given a fairly formal setup: they were told to sit at the table and instructed to focus on the task. The other half were allowed to sit on the floor and given encouragement rather than instructions. While the floor-sitting group *seemed* more distracted and unfocused, they were much quicker to solve the puzzles than those who had 'studied' them.

Play may look silly, chaotic or meaningless, but it's the way we're wired to learn.

GETTY IMAGES X4

IS SCREEN TIME TRULY BAD FOR CHILDREN?

Like so many things, the poison is in the dose. Studies by Prof Dorothy Singer and Prof Jerome Singer, child development experts at the Yale School of Medicine, suggest that watching educational shows (and discussing them afterwards) are great for children's vocabulary.

We shouldn't be overly worried about gaming either. A 2019 study of 180 adolescents found that those who played cooperative online games with friends had stronger, healthier friendships after a gaming session – although competitive games tended to damage feelings of friendship, at least temporarily.

There's one type of screen use that is harmful: our own. Research from an international study in 2012 strongly suggests that the more time we, as parents, spend in front of screens, the less time we spend interacting with our children. In turn, this slows down their social, cognitive and linguistic development. It's definitely worth making time for device-free dinners and screenless socialising with your kids.

DOES 'BABY TALK' MAKE A CHILD SMARTER?

While humans come into the world more dependent than any other mammal, our hearing is surprisingly advanced. Studies show that babies have learned the rhythms of their maternal language some time in the final few weeks of their stay in the womb.

Babies are born listeners, but their ability to express themselves can only develop with our help and that means a couple of years of highly repetitive 'baby talk'.

The patterns of infant- and child-directed speech are linguistically very sophisticated. Studies from the mid-20th Century show that caregivers tend to follow an almost universal set of stages when speaking to their children. First come the repetitive one- or two-word phrases ("Look! Doggy." "Nice doggy."). As babies master those single words, caregivers start to make their sentences slightly longer ("Look at the doggy."). And then, as short sentences are mastered, we start to add abstract concepts such as sensations, then emotions, then beliefs and desires.

When you unselfconsciously use 'baby talk' you're providing your child with a perfectly graduated linguistic apprenticeship, so keep on talking!

WHAT IS THE BIGGEST PARENTING MYTH?

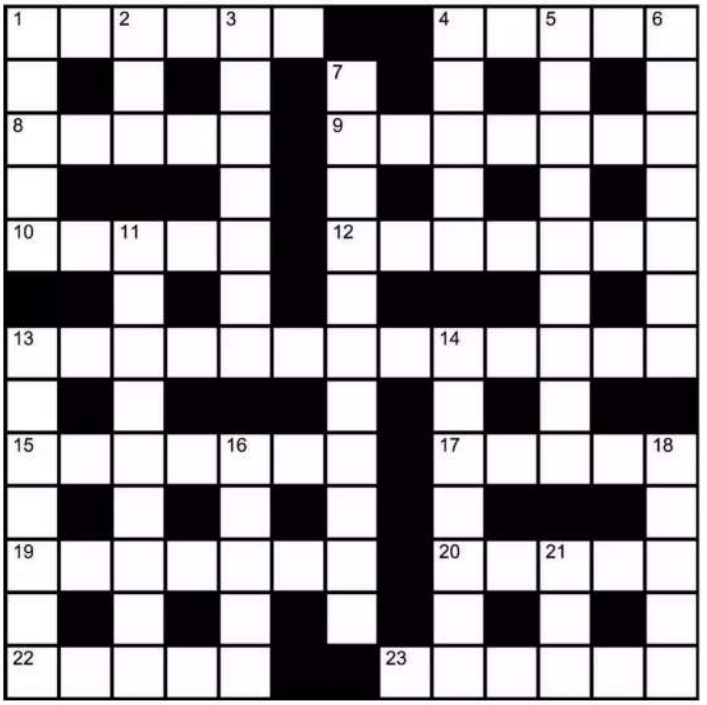
That you have to be perfect. No one has a foolproof recipe for raising your child because they – and you – are unique. That means parenting, like scientific research, involves a lot of trial and error. Make amends when you make mistakes. And stay curious, creative and compassionate.

by EMMA BYRNE

Emma is science broadcaster and author of How To Build A Human: What Science Knows About Childhood *(£14.99, Profile Books).*

CROSSWORD

GIVE YOUR BRAIN A WORKOUT



ACROSS

1 Space for a victory in an urban area (6)
4 He gets up part of stairs (5)
8 Intended to have miserly time (5)
9 Costume remaining the same (7)
10 Like a writer, no evergreen (5)
12 Arranged loan with zero return – just a bit of wool (7)
13 Returned to list previous works (4,9)
15 Mary rewrote a book on an insect (4,3)
17 Get rid of a channel (5)
19 Title of the French king overturning fashion (7)
20 Characteristic art, transforming object (5)
22 Returning, say, taking road for some distance (5)
23 Look for son and reach out (6)

DOWN

1 Mark finds a butterfly (5)
2 By way of answer, six went first (3)
3 Huge bird I can broadcast (7)
4 Rule in bad conditions, say (5)
5 Direct attention to strange plot in vision (9)
6 Old empire church book (7)
7 Feature, on occasion, the giving of attention (7,4)
11 Runner that gives hearty encouragement (9)
13 Past is repeated – also included, eventually (2-3-2)
14 Nowadays allow out the heartless, coarse girl (7)
16 Danes out of range (5)
18 Shut chains around cage (5)
21 Couple not beginning in tune (3)

ANSWERS

For the answers, visit **bit.ly/BBCFocusCW**
Please be aware the website address is case-sensitive.

NEXT ISSUE

DREAM ENGINEERING

Is it possible to change what you experience when your head hits the pillow?

GETTY IMAGES

PLUS

I FEEL THE NEED. THE NEED FOR SPEED

Inside the cockpit of NASA's new X-59 QueSST, which travels faster than the speed of sound.

THE EXPLAINER

What is light?

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POPCORN SCIENCE

How smart could video game AI get?

Will we want non-player characters in video games to think, feel and interact, like in new movie *Free Guy*?

by STEPHEN KELLY

A non-player character, or NPC, is any character in a video game who is not directly controlled by you, the player. It's the zombie you shoot in the face in *The Last of Us*. It's the innocent bystander you hit while speeding in *Grand Theft Auto V*. It's the capitalist racoon who enslaves you into a lifetime of debt in *Animal Crossing*. They are often characterised by a lack of agency and depth: a result of them being restricted by a set of pre-determined choices and algorithms. But artificial intelligence is getting smarter – and NPCs are too.

New movie *Free Guy* takes this to its most extreme conclusion, positing a scenario in which an NPC (played by Ryan Reynolds) gains self-awareness in a huge *Grand Theft Auto*-style video game. No longer is he a puppet with a set of stock phrases, but he can think, feel and interact. Surely this is the future of gaming?

"The chances of an NPC becoming self-aware are virtually zero," says Dr Edward Powley, associate professor of artificial intelligence in Falmouth University's Games Academy. "Creativity, consciousness, self-awareness – we might be able to create the illusion of some of these, but achieving them in any meaningful way is still decades away, partly because our understanding of how the human brain does these things is still very limited."

But that doesn't mean that game developers are not experimenting with AI. In 2020, game developer Ubisoft released *Watch Dogs: Legion*, which populated its dystopian recreation of London with some of the most dynamic and idiosyncratic NPCs ever seen. To achieve this, they built Census, a complex system that generates biographies, relationships and narratives for the city's NPCs population. Save a man from police brutality one day, and he and his brother may become your allies the next… or your enemies, if you accidentally injure their best friend in a firefight.

In terms of the future, the tech that Powley is most interested in is natural language processing. "This is behind systems such as Alexa and Siri, which allows you to interact with a computer system using plain English." The potential for video games is reactive NPCs who can hold a real-time conversation with the player as they type sentences or speak into a microphone. The most cutting-edge example so far is 2005 video game *Façade*, in which the player has to navigate a cocktail party without saying the wrong thing and being thrown out. "The technology needs to advance further to be truly feasible in games," says Powley.

There is a risk that such technology could compromise authorial control. This is Powley's concern with methods such as machine learning, which allow AI to analyse data, interpret it, and make its own decisions. This could lead to NPCs who behave with more freedom and flexibility. But leaving aside the fact that it would require a lot of time and computational power, there's also the question of whether 'better' NPCs would make for better video games.

"Video games are all about telling a story or giving the player an experience, and NPCs being too unpredictable can break that," says Powley. "A lot of what we do when we play games is about figuring out systems, and NPCs that are too unpredictable are too difficult to figure out." **SF**

***Free Guy* is released in UK cinemas 13 August 2021.**

VERDICT

While intriguing, the AI underlining *Free Guy* is neither possible nor desirable.

by STEPHEN KELLY (@StephenPKelly)
Stephen is a culture and science writer, specialising in television and film.

ILLUSTRATIONS: ADAM GALE. MAIN ILLUSTRATION: JOE WALDRON

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